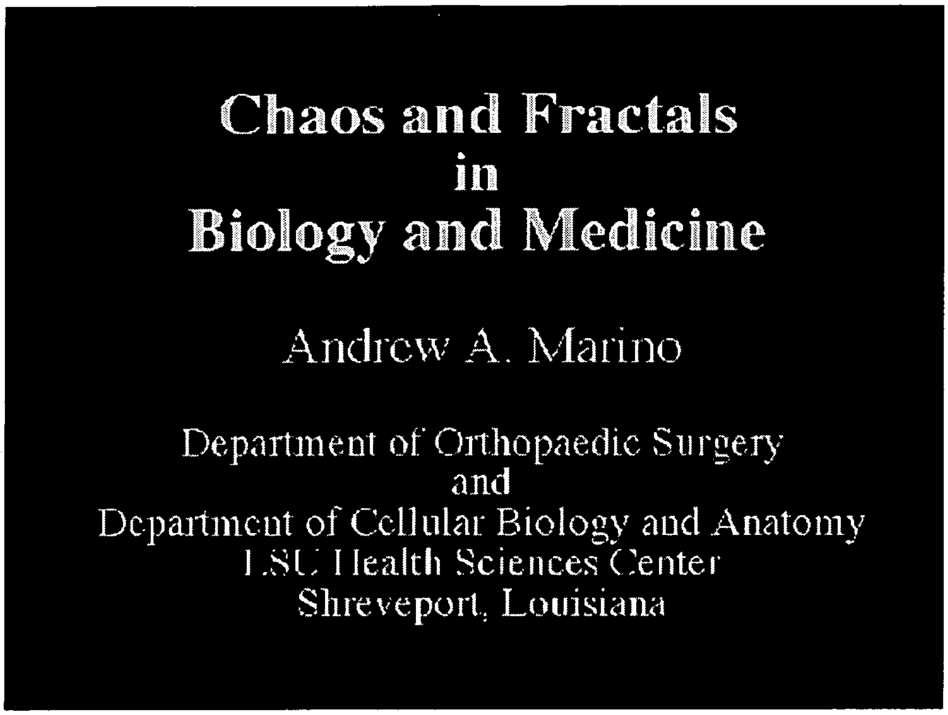
TEMPLE 2000 PRESENTATION

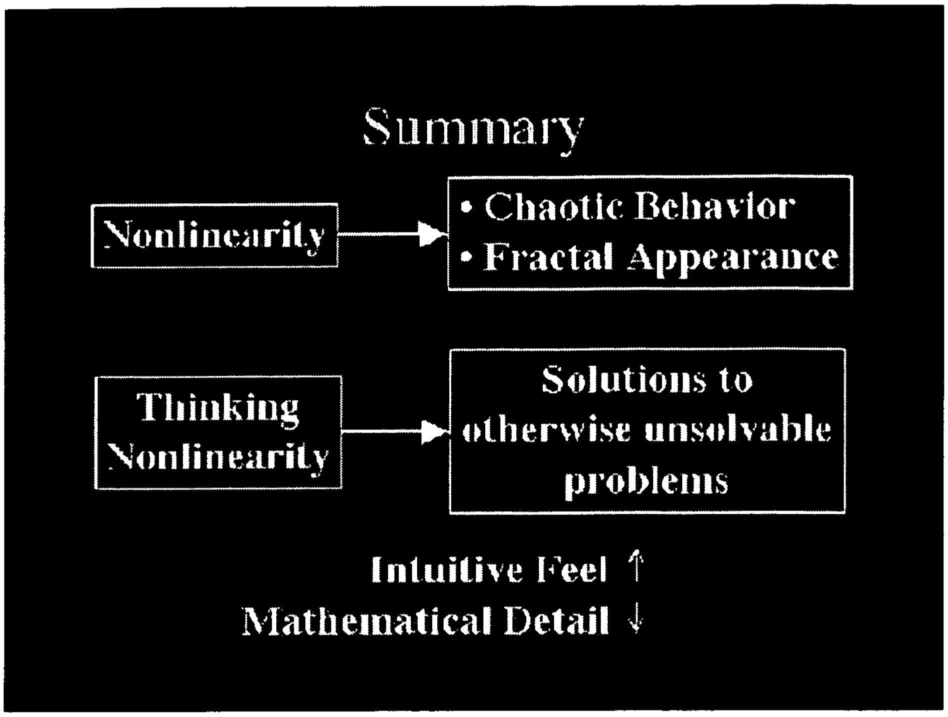
http://www.ortho.lsumc.edu/Faculty/Marino/Temple/Temple.html

Slide 1: Title



Despite the successes of 20th-century science, many important problems remain unsolved. As examples, we do not know what causes cancer or other diseases, we cannot predict when heart attacks or strokes will occur, and we do not know how information regarding shape and appearance is stored or transmitted. It is becoming more clear that answers to these and other questions require a reformulation of our world view to include the existence of nonlinearity and, in particular, the occurrence of deterministic chaos. The purpose of this presentation is to describe the inherent limitations of the present scientific paradigm, and to indicate how some important scientific problems might be satisfactorily resolved by looking at the world in a nonlinear way. In my view, one such problem involves an understanding of the mechanistic basis by which environmental electromagnetic fields can give rise to health hazards. Resolution of the EMF hazards issue was used as a particular example of the power of biological nonlinearity to explain the meaning of bona fide data.

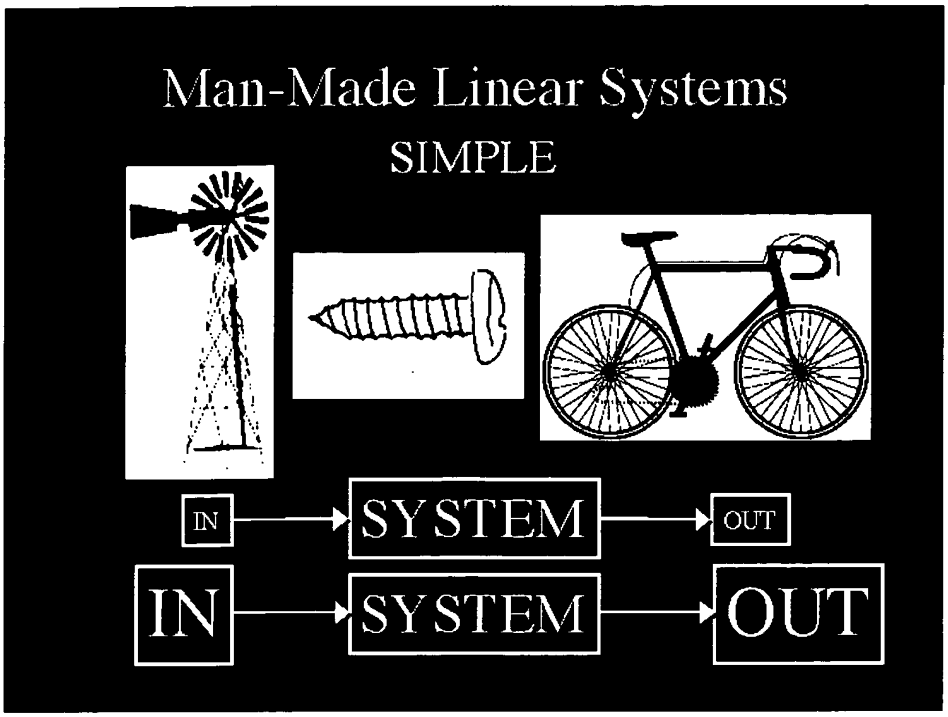
Slide 2: Summary



In some contexts, nonlinearity simply means non-straight-line change. As used here, it will mean behavior or structure that looks random or complex but which really isn't, and can be recognized as deterministic when examined in the proper way. I will conclude that nonlinear systems give rise to this kind of behavior, called chaotic behavior, and that its signature is a fractal. Further, I will show that thinking in a nonlinear way can potentially lead to solutions to problems not otherwise solvable.

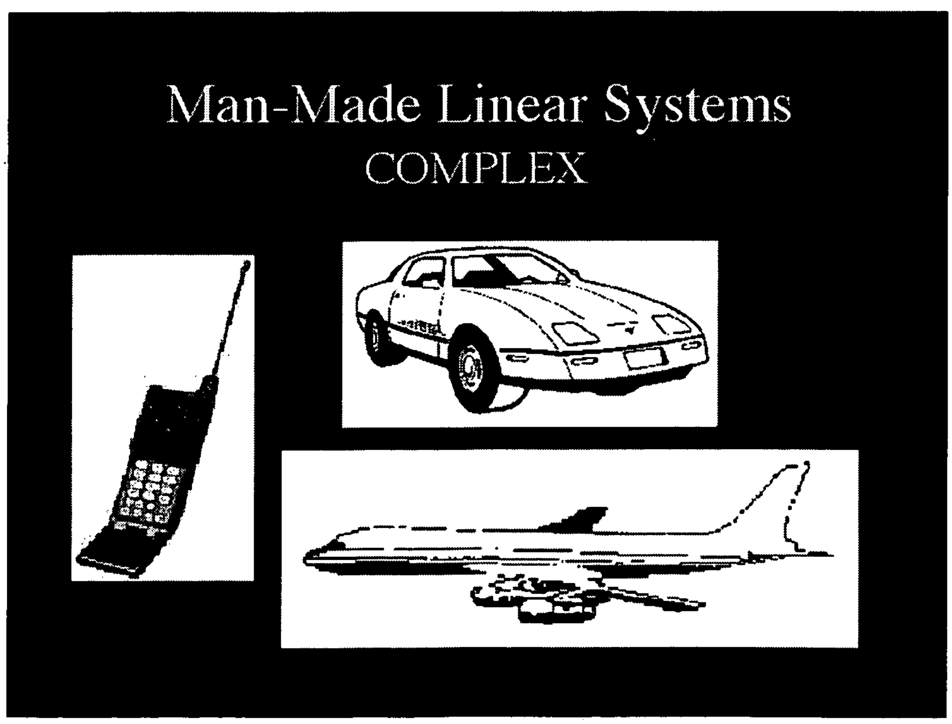
Throughout the talk, the emphasis will be on attempting to foster a feeling for the power and significance of nonlinearity in biology. I will omit almost all of the mathematical detail.

Slide 3: Man-Made Linear Systems (Simple)



Almost everything man builds is linear in nature because linearity entails predictability. Devices that aren't predictable generally aren't useful. The basic property of a linear system is that a small input leads to a small output, and a large input leads to a large output. If you pedal the bike at a certain rate, for example, you move at a certain speed. If you pedal slightly faster, you move slightly faster. Man's machines tend to work that way.

Slide 4: Man-Made Linear Systems (Complex)



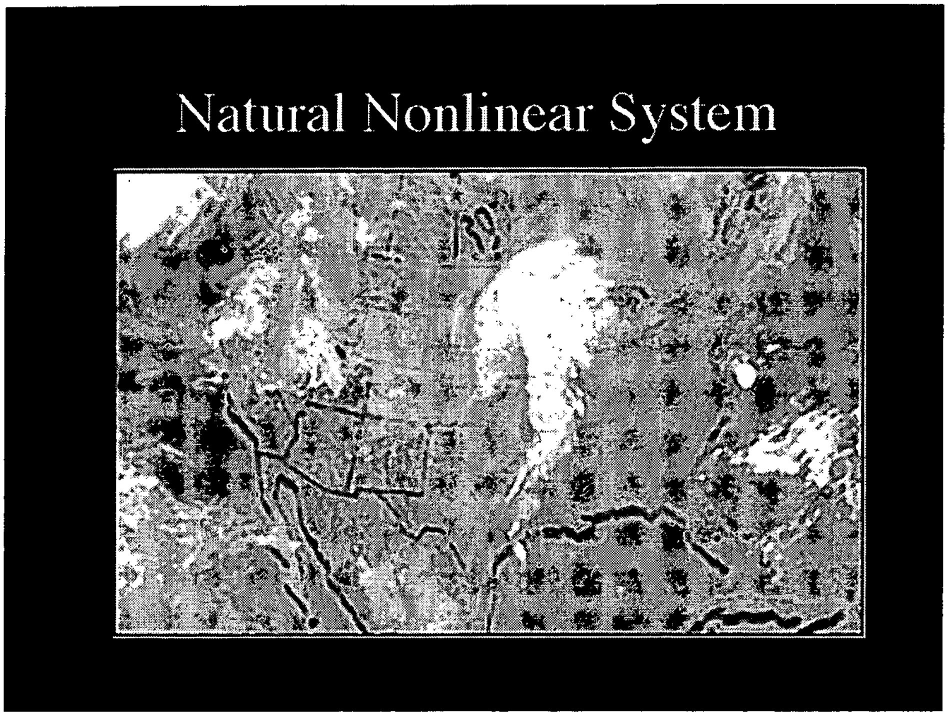
Not all linear systems are simple. There are many links, for example, between the amount the accelerator is

depressed and the speed of an automobile. Nevertheless, considered as an input-output device, even the automobile and other complex devices that man builds are linear devices.

Slide 5: Man-Made Nonlinear System

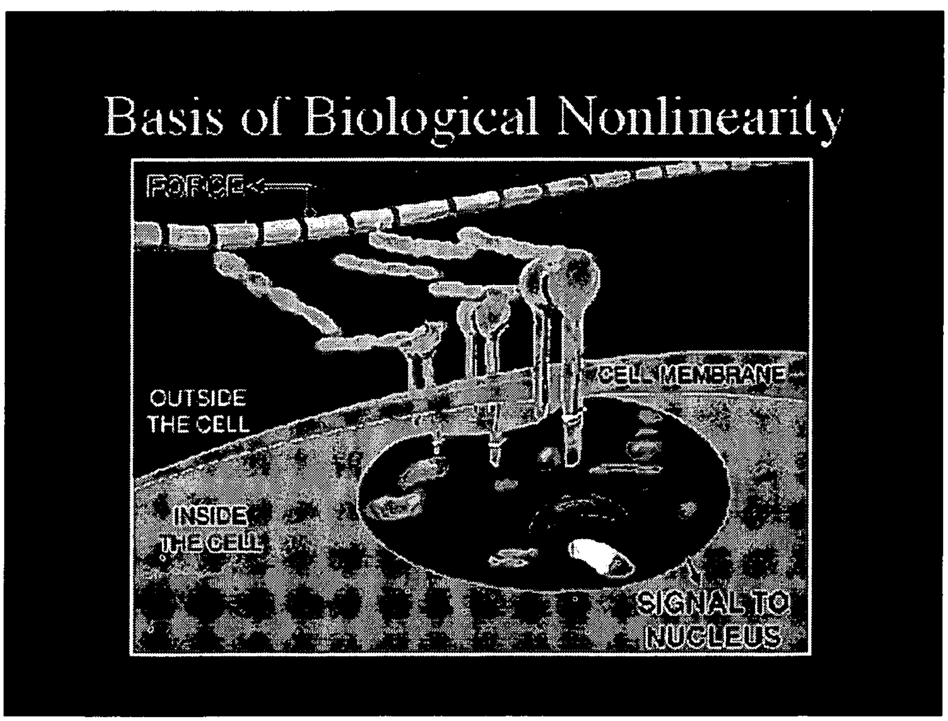
Sometimes we build nonlinear systems for fun. The attraction of a lava lamp, for example, is precisely its unpredictability. It's a simple system - water, wax, and heat. Yet, no two patterns are ever exactly the same.

Slide 6: Natural Nonlinear System



In contrast to what man does, nature frequently builds nonlinear systems. Other than hypothetical devices such as a spring with no friction or a pendulum with no air resistance, essentially every natural system is nonlinear, even though many natural systems can be satisfactorily approximated as linear systems.

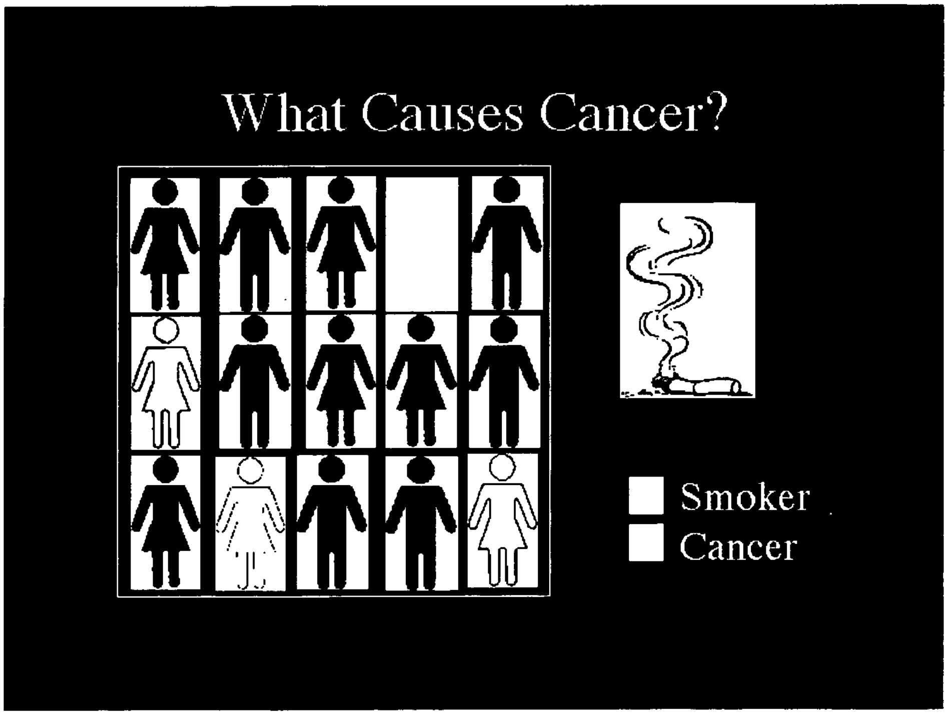
Slide 7: Basis of Biological Nonlinearity



This slide illustrates generally how nonlinearity, that is nonproportionality between input and output comes about in the body. The slide depicts a typical transduction system in the body. Force is transmitted by structural

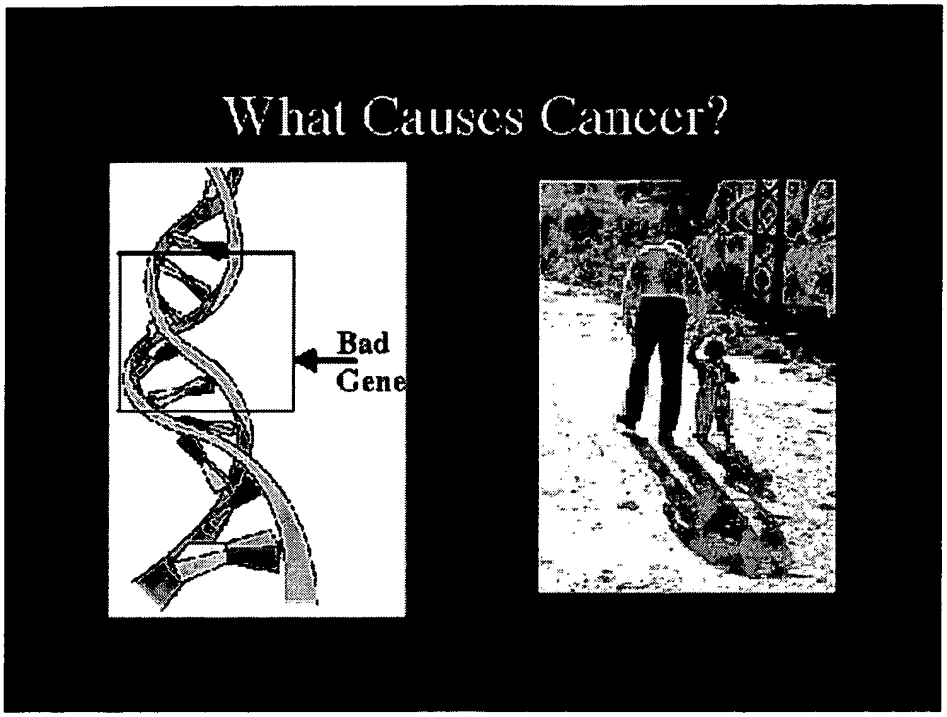
proteins, some of which are connected to proteins embedded in the membranes of cells. The intracellular portion of the membrane protein is in contact with a group of interacting enzymes that help to convert the external force to a chemical signal which then migrates to the nucleus of the cell and ultimately directs the cell's activity. Thus, the input is force, and the output is one or more proteins that are manufactured by the cell. Within a certain range, a given force corresponds to a certain amount of cell activity, and more or less force corresponds to more or less activity. Suppose that for a particular force, the enzymatic activity of one particular enzyme had the value X, and suppose further that at the moment the enzyme had that value we could directly add more of the enzyme so that the effective level was twice normal. The output of the cell would not be twice. In general, when we alter specific components of complex biological systems the results are unpredictable.

Slide 8: What Causes Cancer?



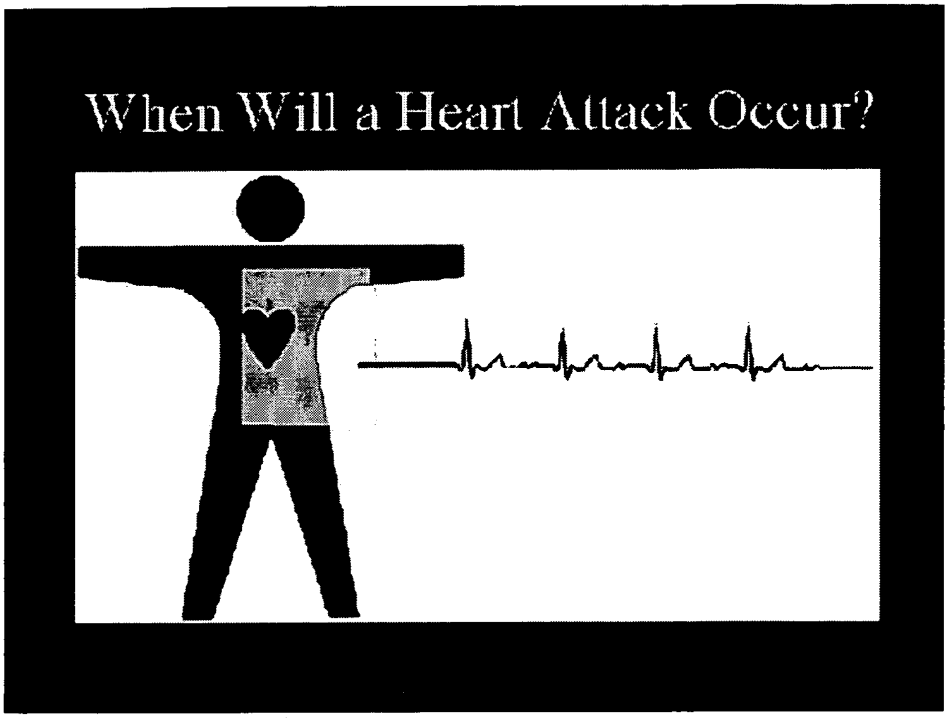
One of the problems that a nonlinear model seems best able to resolve is the problem of what causes disease, cancer for example? It can't be something simple, like smoking, because most people who smoke don't get cancer, and many people who get cancer don't smoke.

Slide 9: What Causes Disease?



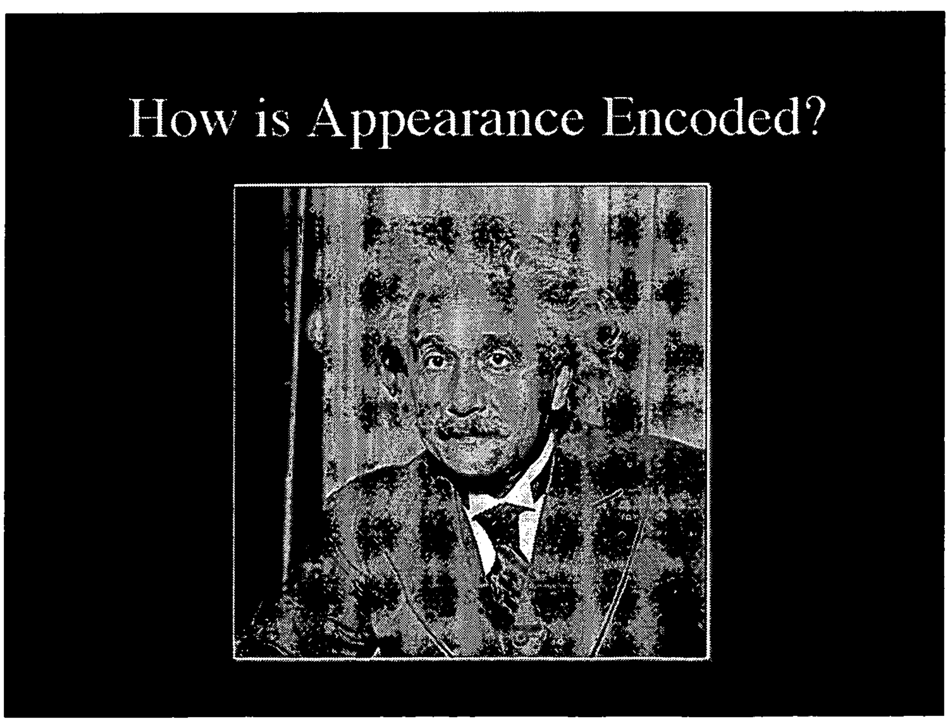
Similarly, it is inaccurate to attribute cancer to the presence of a mutated gene because such an explanation begs the question. Something, for example, must have caused the mutation. We know that the man's shadow was an effect caused by the man, and not vice versa, and it is probably similarly true that mutations found in clinical cancers are effects, not causes. Other factors, called risk factors, are even more tenuously associated with disease. We say, for example, that high cholesterol is a risk factor for coronary artery disease based on evidence of their statistical association. Although we sometimes assume such associations are causal, that need not be the case.

Slide 10: When Will Heart Attacks Occur?



On the basis of a linear model for how biological systems work, it is not possible to predict when a heart attack or an epileptic seizure will occur in a particular individual. Presently, we have no idea how to do it, and no reason to believe that it will ever be possible.

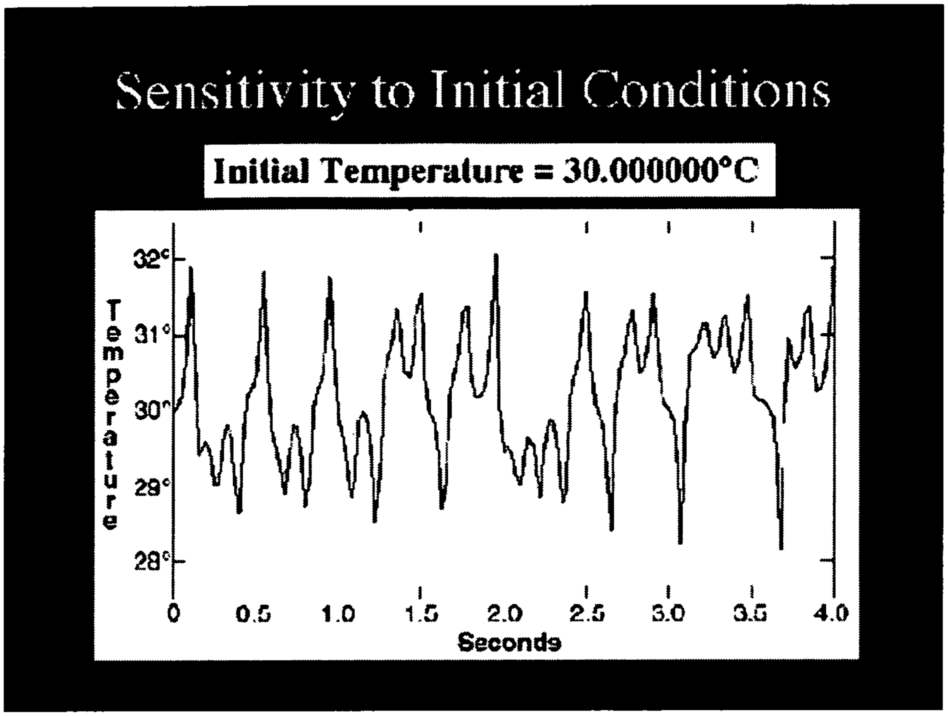
Slide 11: How is Appearance Encoded?



The human genome specifies the code for more than 100,000 proteins, but it does not specify their final arrangement, and there is no explanation for what does. Why do individuals exhibit a particular appearance?

Why, for example, is the difference between Einstein and President Kennedy immediately apparent, even though their genes were identical?

Slide 12: Sensitivity to Initial Conditions (1)

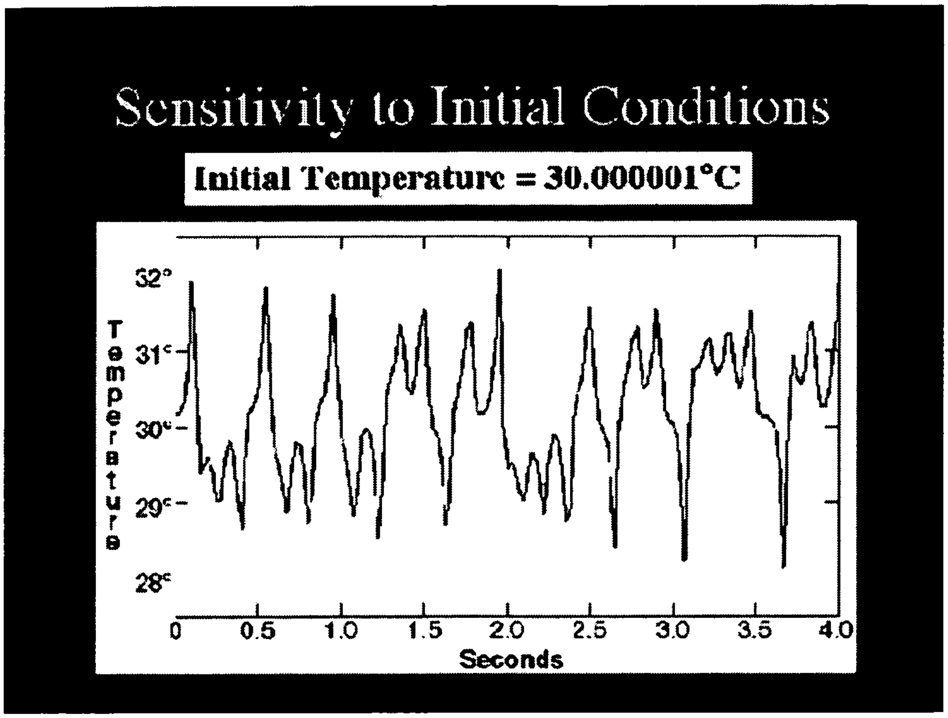


I've described some questions that seem not to be amenable to solution when we look at the world in a linear way. Now, I will focus on some properties of the nonlinear world, and then try to show that these properties may be conducive to solutions to these unsolved problems.

This slide shows 4 seconds of temperature data that I obtained from a group of nonlinear equations commonly used to model changes in the weather. You can see that the temperature changes appear to be random, but as I told you the opposite is true. They are completely predictable because this entire pattern was generated from equations. The first point to recognize, therefore, is that a nonlinear system may look as if it is behaving randomly, even though the opposite is true.

Now I want to make a second point about nonlinear systems. An important point. An equation, linear or nonlinear, can predict the future of a system only if the starting point is specified. In this slide, I chose the initial temperature as indicated. For that choice of initial condition, the system evolved as depicted.

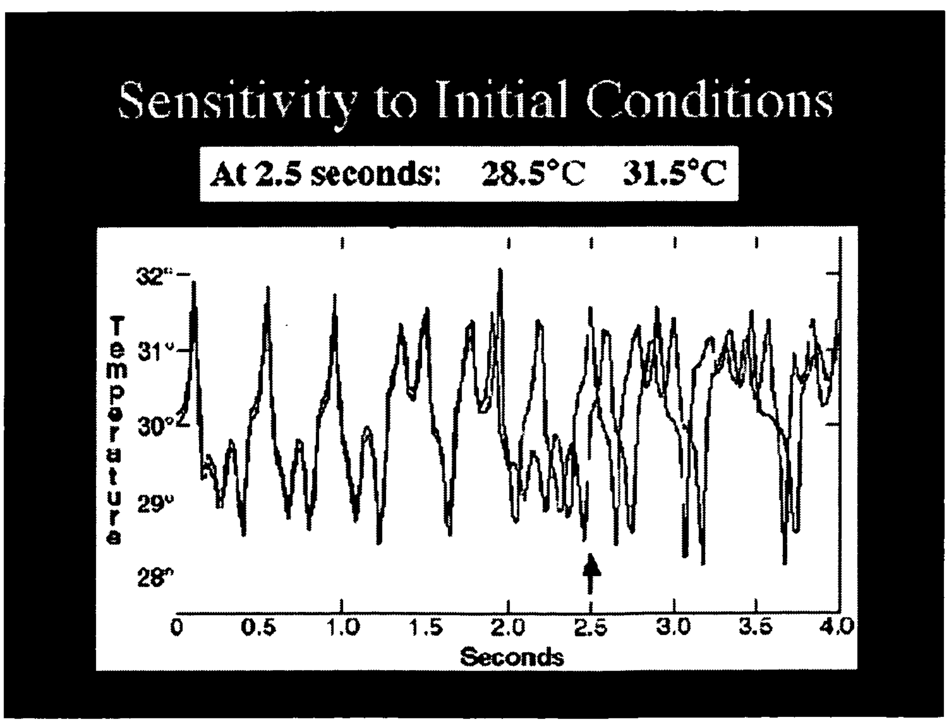
Slide 13: Sensitivity to Initial Conditions (2)



What happens if I choose a different initial condition? This slide shows the evolution of the same system starting from an initial temperature one millionth of a degree higher than was the case in the previous slide. Again the system looks noisy and irregular.

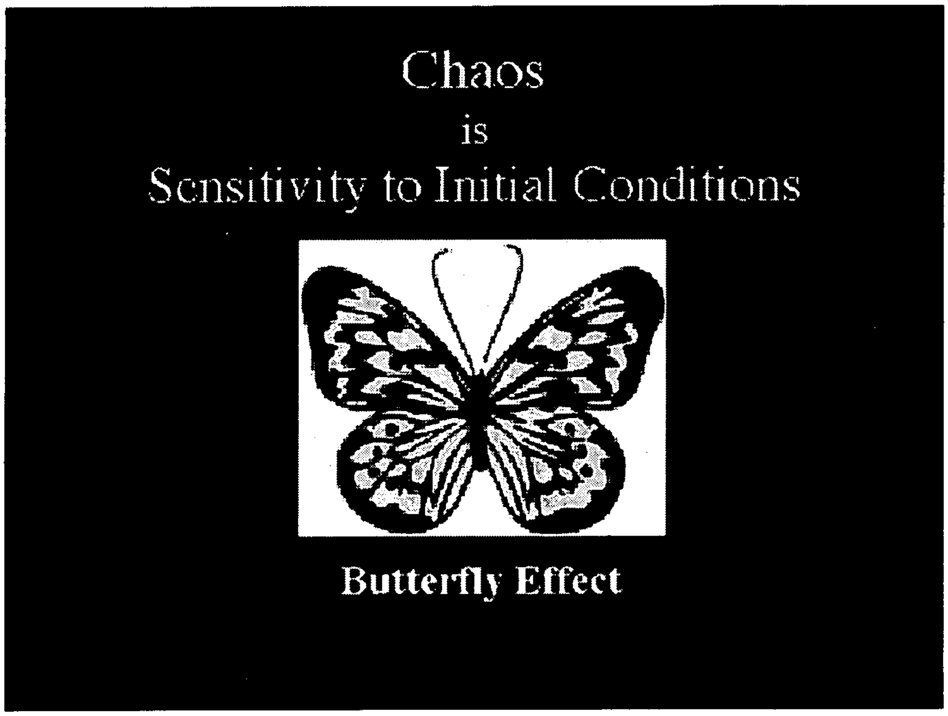
Do the two cases differ?

Slide 14: Sensitivity to Initial Conditions (3)



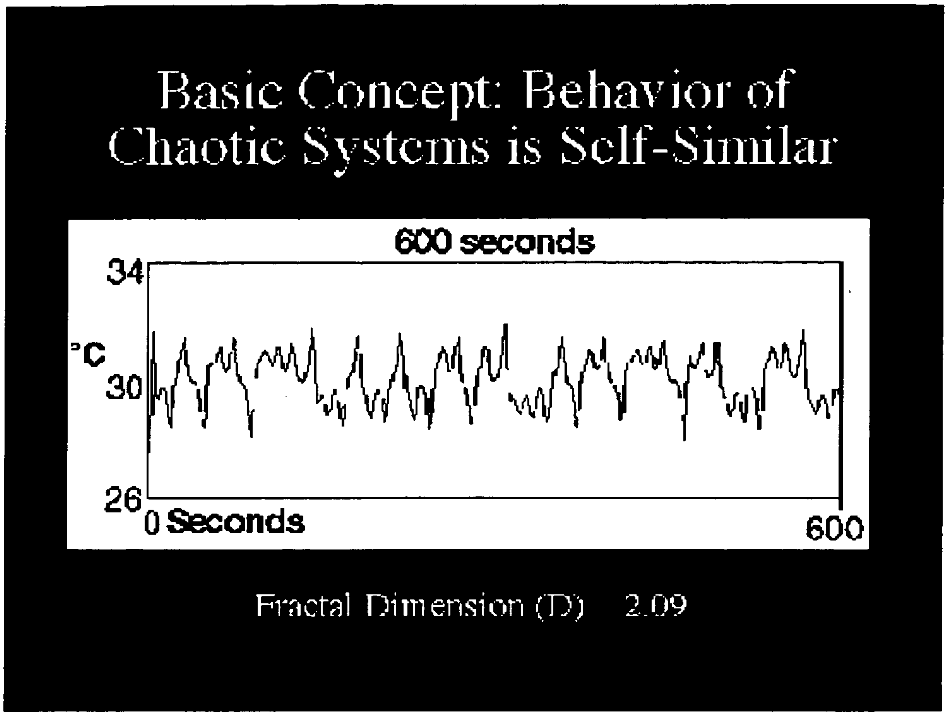
I superimposed the results of the previous two calculations. Note that the two cases initially behaved identically. For about 2 seconds, it simply didn't matter which of the two initial temperatures I chose. Thereafter, synchronization was lost and it remains lost forever. The two cases never look the same again. Thus, at 2.5 seconds, someone observing the first system would record its temperature as 28.5°C, whereas an observer of the second system would record 31.5°C. The difference in temperature of the two systems would therefore be about 3°C, despite the fact that the initial difference between the systems was unimaginably small and physically unrealizable. This property is called sensitivity to initial conditions, or deterministic chaos, and it is a property exhibited solely by nonlinear systems.

Slide 15: Chaos is Sensitivity to Initial Conditions



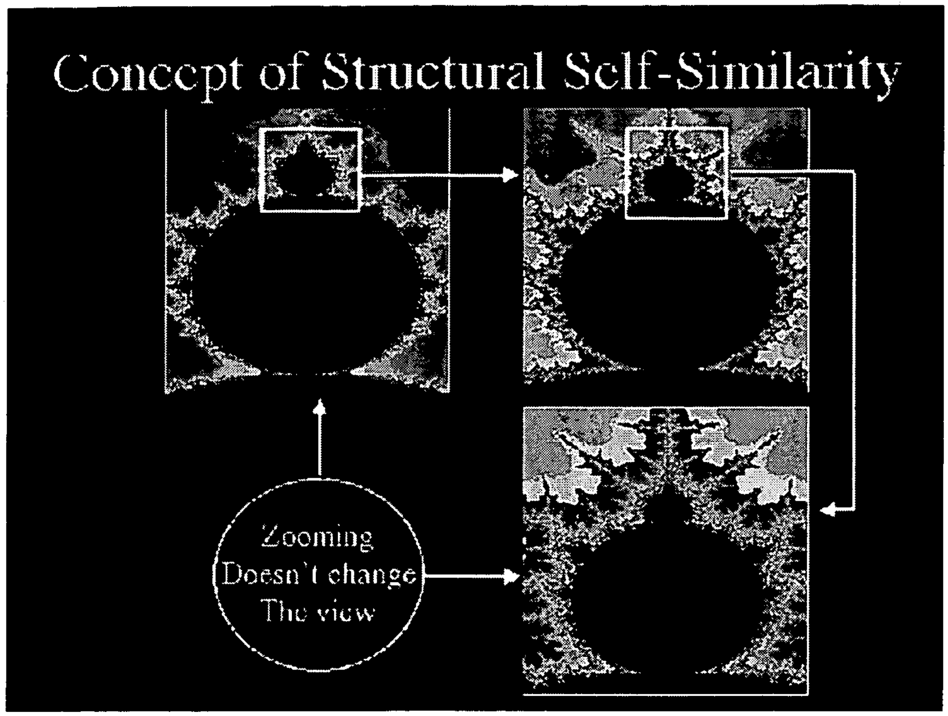
A popular name for deterministic chaos is the Butterfly Effect. The notion is that a butterfly flapping its wings in the southern hemisphere could give rise to a hurricane in the northern hemisphere. In the nonlinear world, such an effect is possible because infinitesimally small inputs can have enormous consequences when the underlying system follows nonlinear laws.

Slide 16: Basic Concept: Behavior of Chaotic Systems is Self-Similar



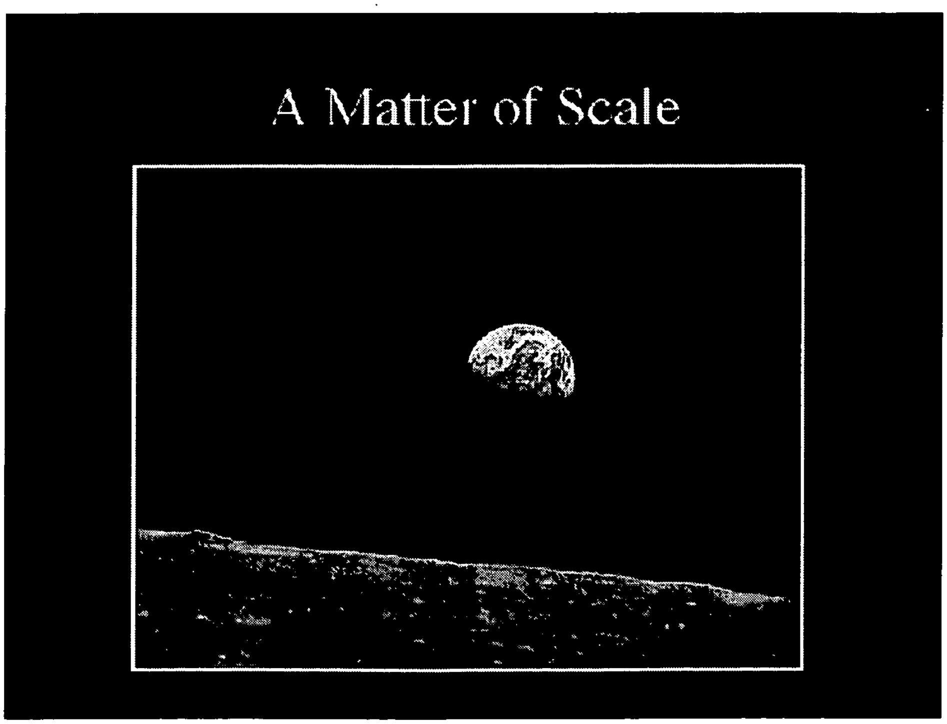
There is another important property of nonlinear systems. The panel shows 600 seconds' worth of data from the temperature model that I mentioned a few moments ago. The pattern looks very much the same at different time scales. The property of appearing identical at different time scales is called self-similarity. There are mathematical methods that can precisely characterize the property of self-similarity in terms of a parameter called "dimension." The dimension for this signal, for example, is 2.09. Note that the dimension is not a whole number, but rather a fraction, and a fractional dimension is frequently called a "fractal." Thus, self-similarity is characterized by a fractal dimension, in this case, 2.09.

Slide 17: Concept of Structural Self-Similarity



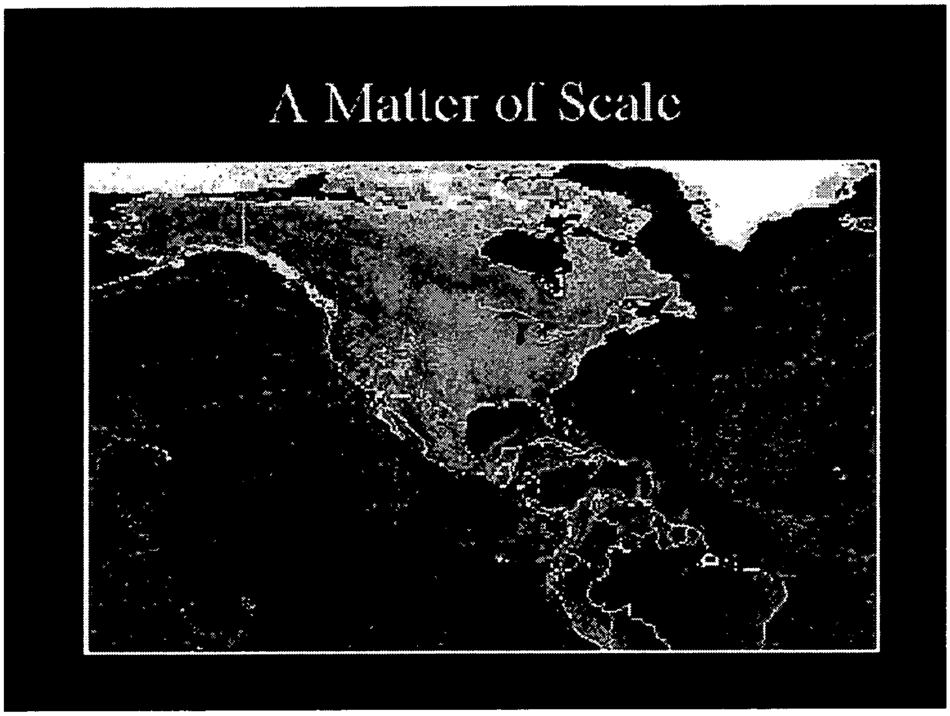
Not only time-dependent behaviors exhibit self-similarity. It can also be found in structures. This structure, which happens to be generated by a mathematical equation, exhibits the property of structural self-similarity. When I focused on a particular region of the structure and enlarged it, the view was the same as that found at lower magnification levels. This slide depicts the process at three successive levels of magnification. I could have repeated this process infinitely many times, and the result would have been that the view is always essentially the same.

Slide 18: A Matter of Scale (1)



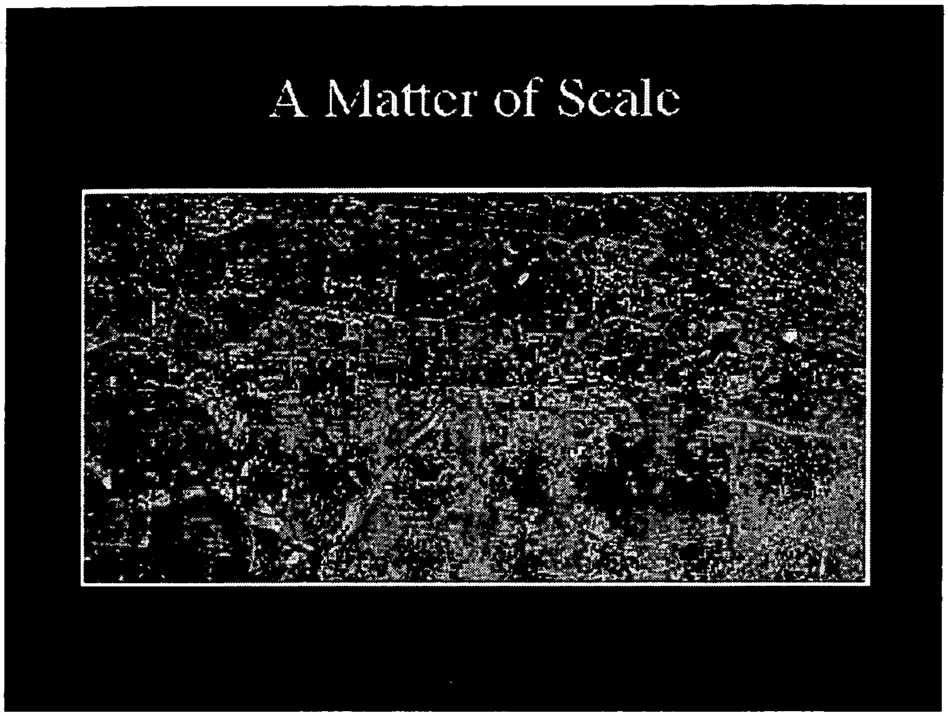
I want to emphasize what an unusual property self-similarity is. It is not unusual in the sense that it is rarely found in nature. I will shortly show you that it is actually very common. Rather, it is unusual because we do not normally recognize it. We are conditioned to think of the view of an object as heavily dependent on the scale of observation. The next series of slides shows that this is the case. This slide shows the earth as seen from the moon.

Slide 19: A Matter of Scale (2)



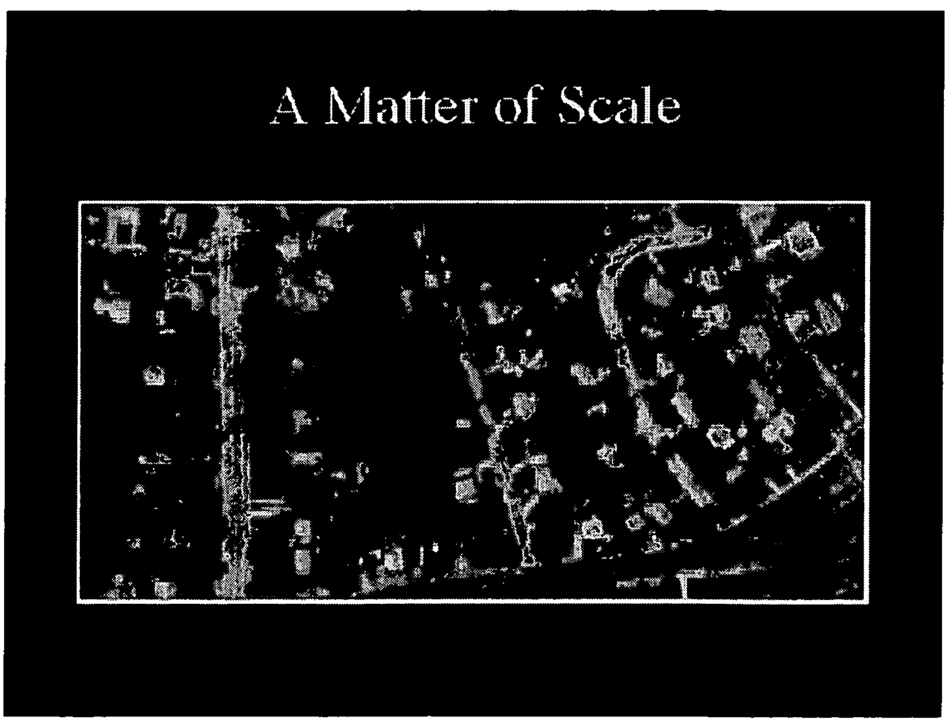
As we zoom in we begin to see structure that was not apparent to the eye while standing on the moon. For example, the outline of the continents can be seen distinctly.

Slide 20: A Matter of Scale (3)



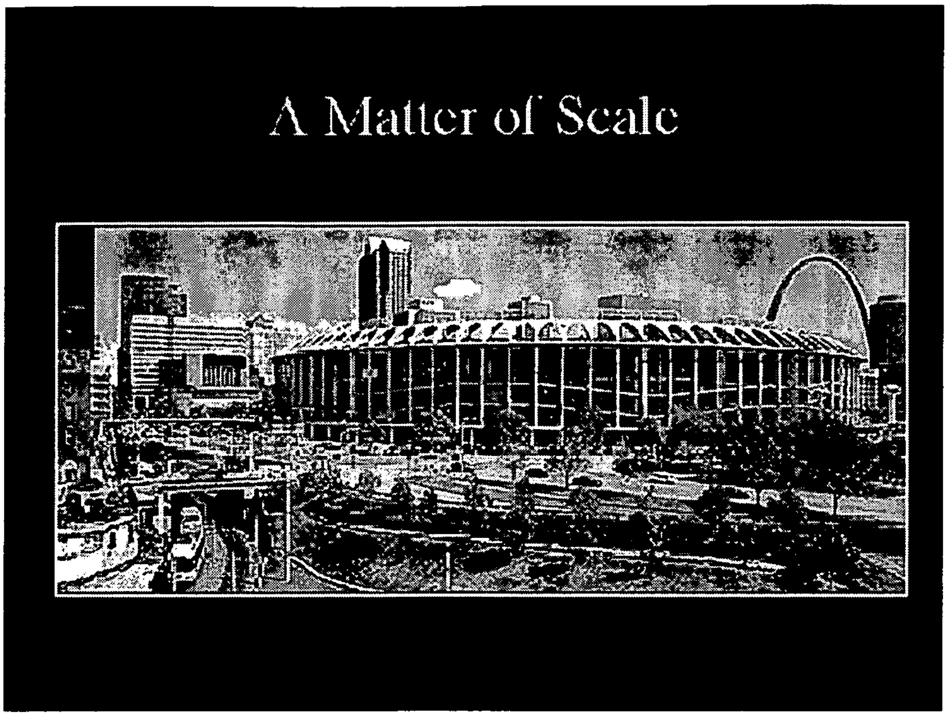
As we continue to zoom in, the coastal detail fades but we begin to see geometric patterns, characteristic of human activity.

Slide 21: A Matter of Scale (4)



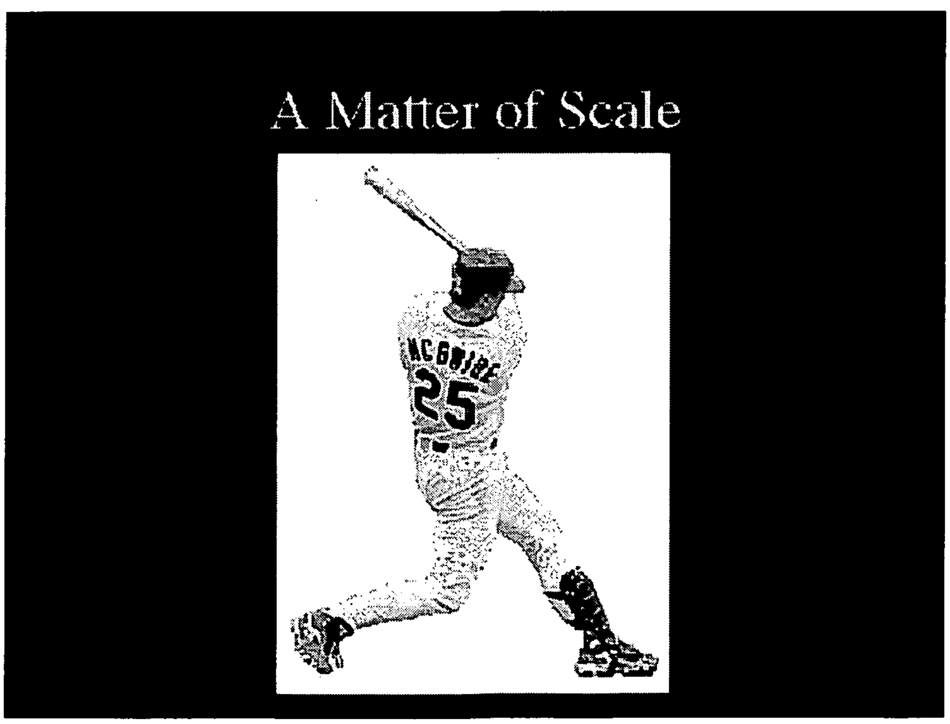
As the magnification increases, new details become apparent.

Slide 22: A Matter of Scale (5)



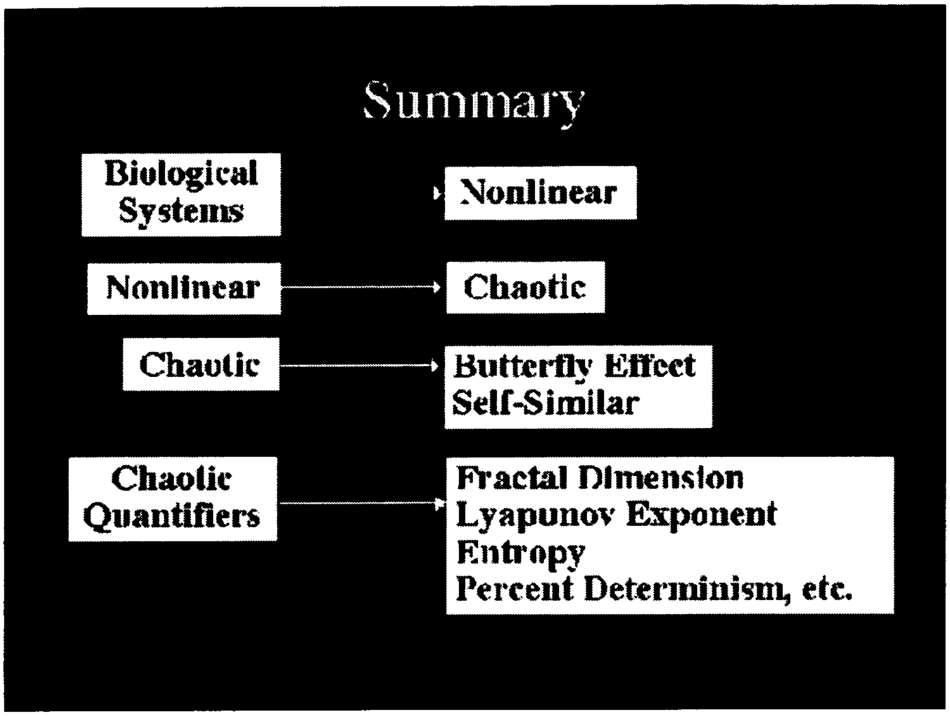
At still further magnification, individual man-made structures become easily perceivable. In this case, for example, Sportsmen's Field in St. Louis. Note that continuing magnification is associated with the appearance of new structure.

Slide 23: A Matter of Scale (6)



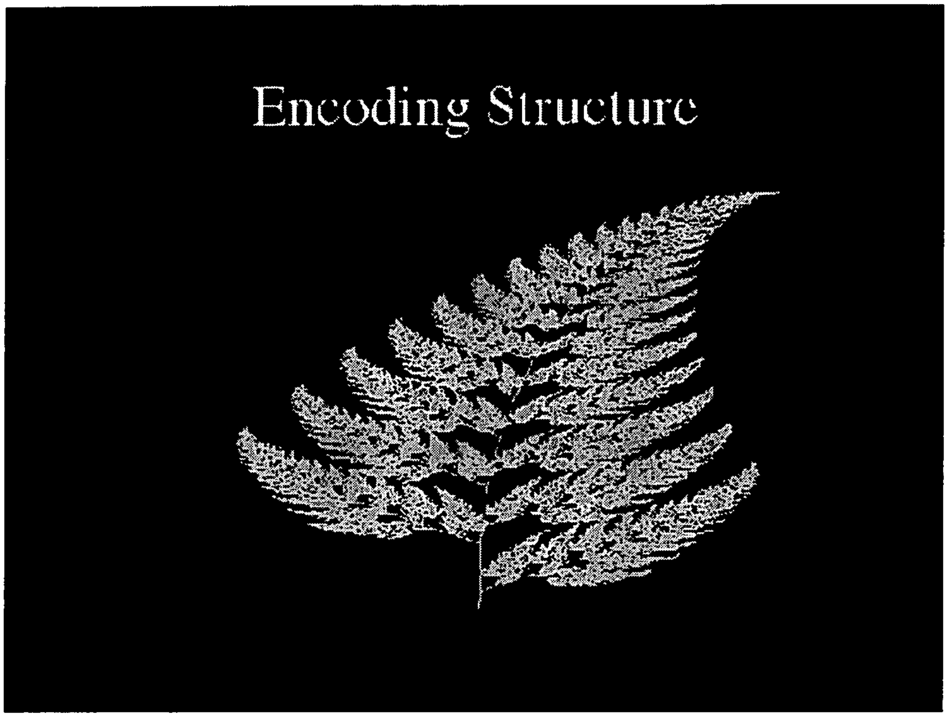
At this level of magnification we can discern individual human activity. All of this scale-dependent appearance seems entirely natural and normal, and it is hard to visualize behaviors or structures that do not have this property. But as I have shown you, objects called fractals do not have that property.

Slide 24: Summary



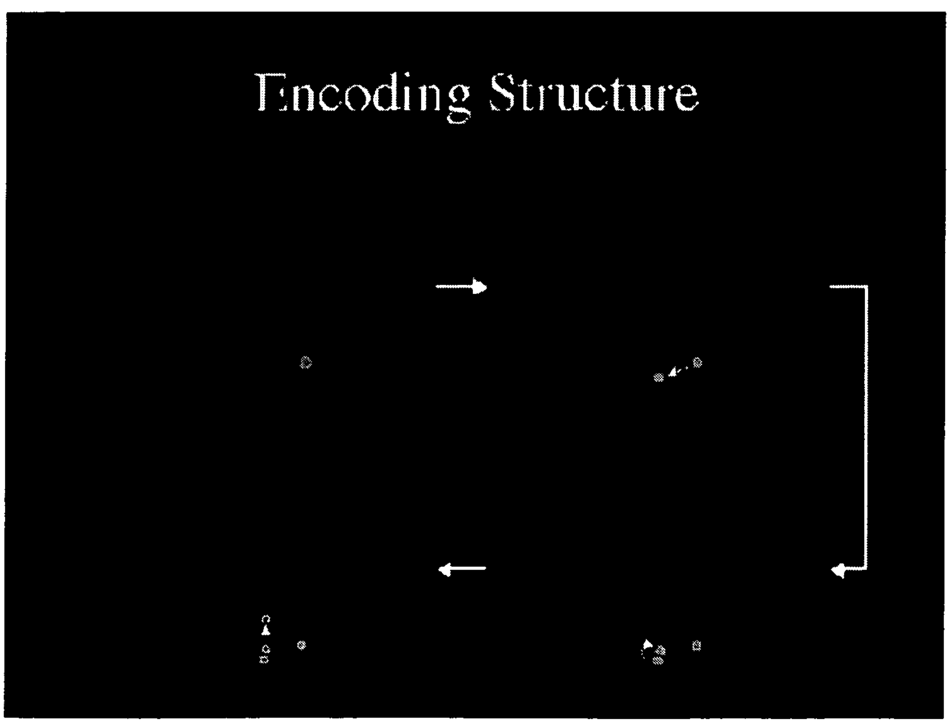
Before I turn to a consideration of particular problems, I want to mention again the concepts I have introduced. Biological systems are nonlinear, nonlinear systems can be chaotic, chaotic systems display sensitivity to initial conditions and self-similarity. These properties can be quantified using standard mathematical techniques. I mentioned fractal dimension, but there are many other quantifiers, a few of which are listed here.

Slide 25: Encoding Structure (1)



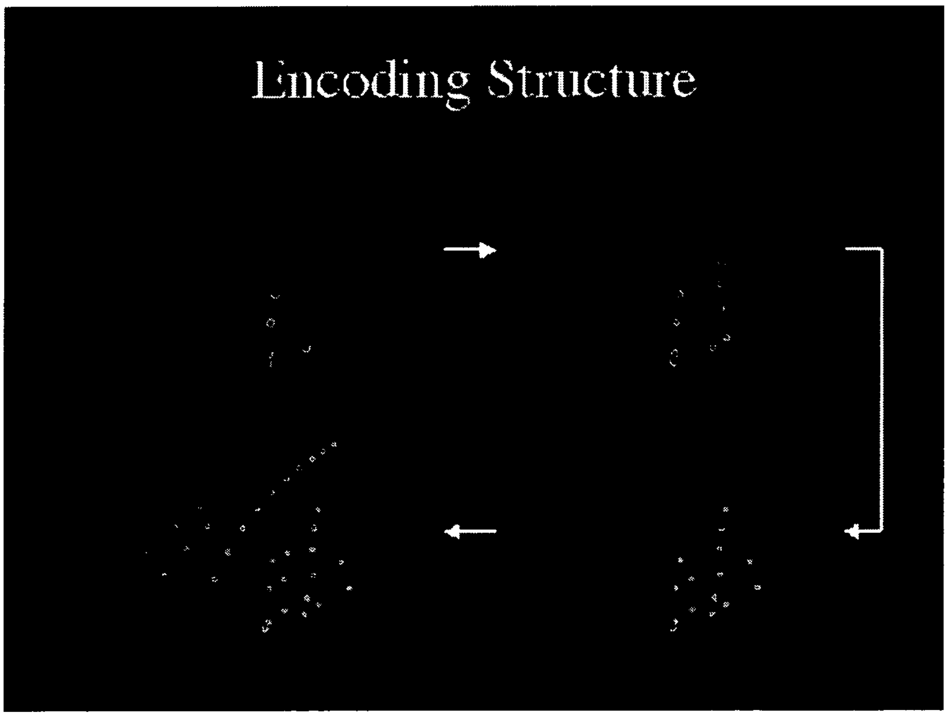
Now, I want to consider some problems that may be amenable to nonlinear thinking. Suppose you wanted to specify or define a complicated biological object, this fern, for example. You can see it is a complex structure and traditional linear models cannot begin to explain where the information that specifies this object is stored prior to the elaboration of the object. We think it must be somewhere, or else how did the object come about? But where? Nonlinear thinking provides a possible answer, and I'm going to use simple mathematical tricks to illustrate this point.

Slide 26: Encoding Structure (2)



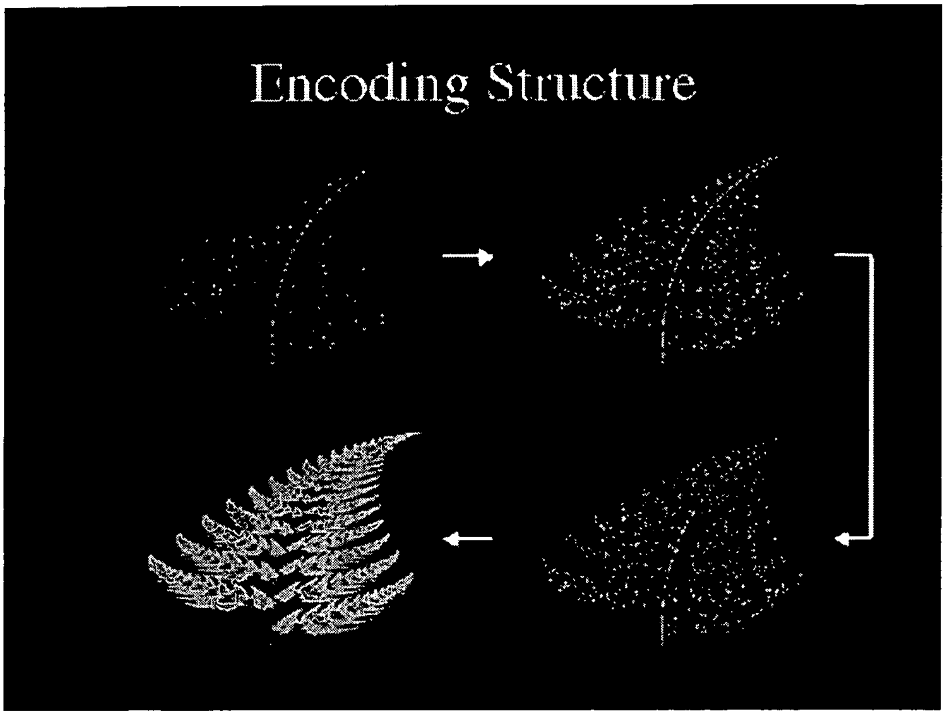
Suppose I start at a point, for example the green dot in the upper left panel, and I adopt 4 rules, each consisting of the movement of the dot in a fixed direction by a fixed amount. In the second panel, for example, I move the dot down and to the left, and I plotted both the original point and the new point. Movement in that direction by that amount is one of the rules, and it was chosen randomly from among the four. In the third panel I randomly chose from the same set of four rules and happened to pick a rule that was different than the first rule. In this case I move the dot a smaller amount and in a different direction, upwards and slightly to the right. Again, I plotted the previous positions of the point in addition to the final position. I repeated the process again to generate the fourth panel. What do you think happens when I continue this process, always choosing one of the four rules randomly, plotting the result, and adding it to the previous result? Will I get a random pattern?

Slide 27: Encoding Structure (3)



This slide shows some of the next steps in the series. I have begun omitting showing you pictures of the intermediate steps for simplicity's sake. You can see, however, that a structure may be emerging.

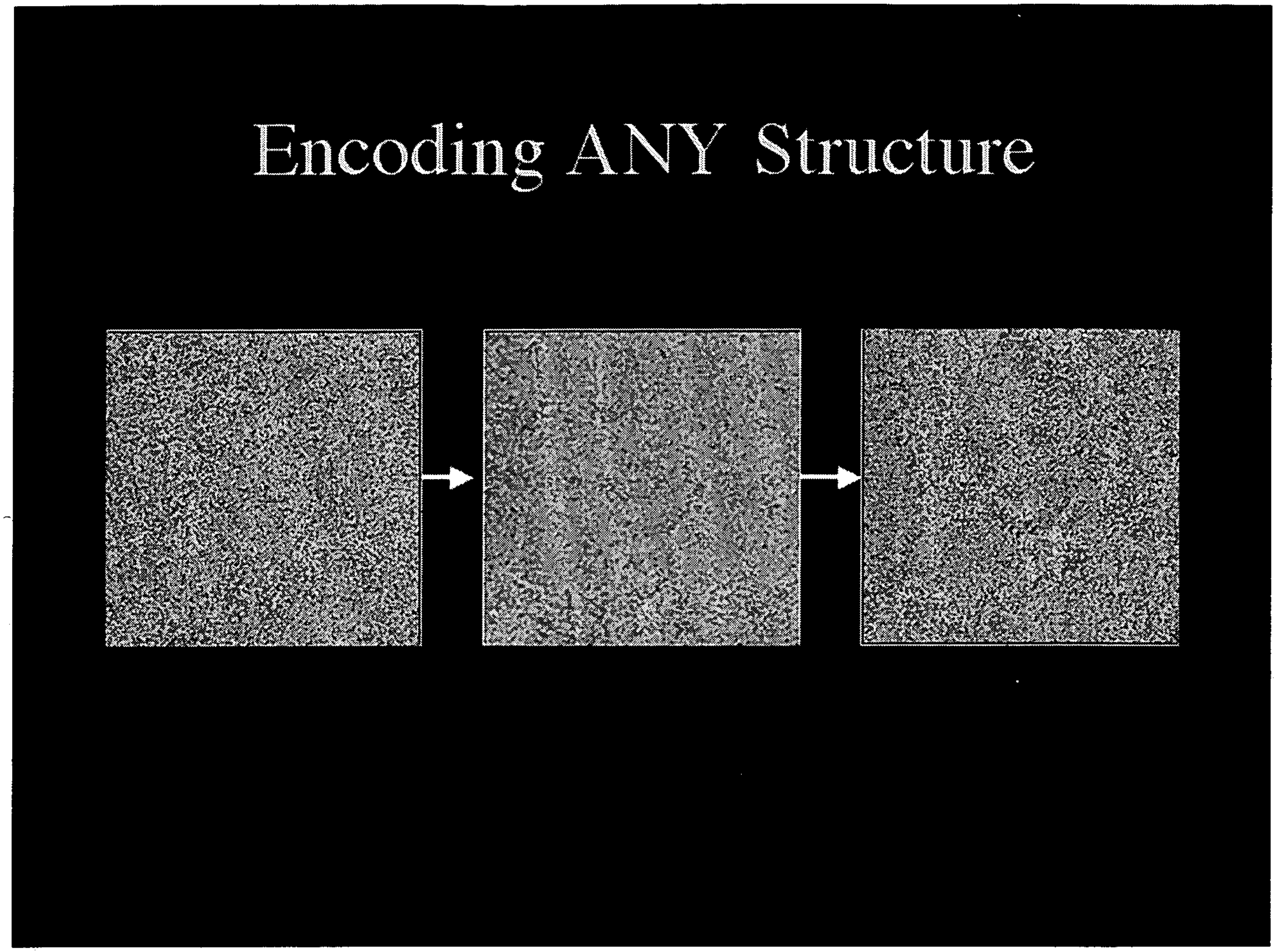
Slide 28: Encoding Structure (4)



This series of panels makes it clear that the process does in fact lead to an organized structure, not a random pattern.

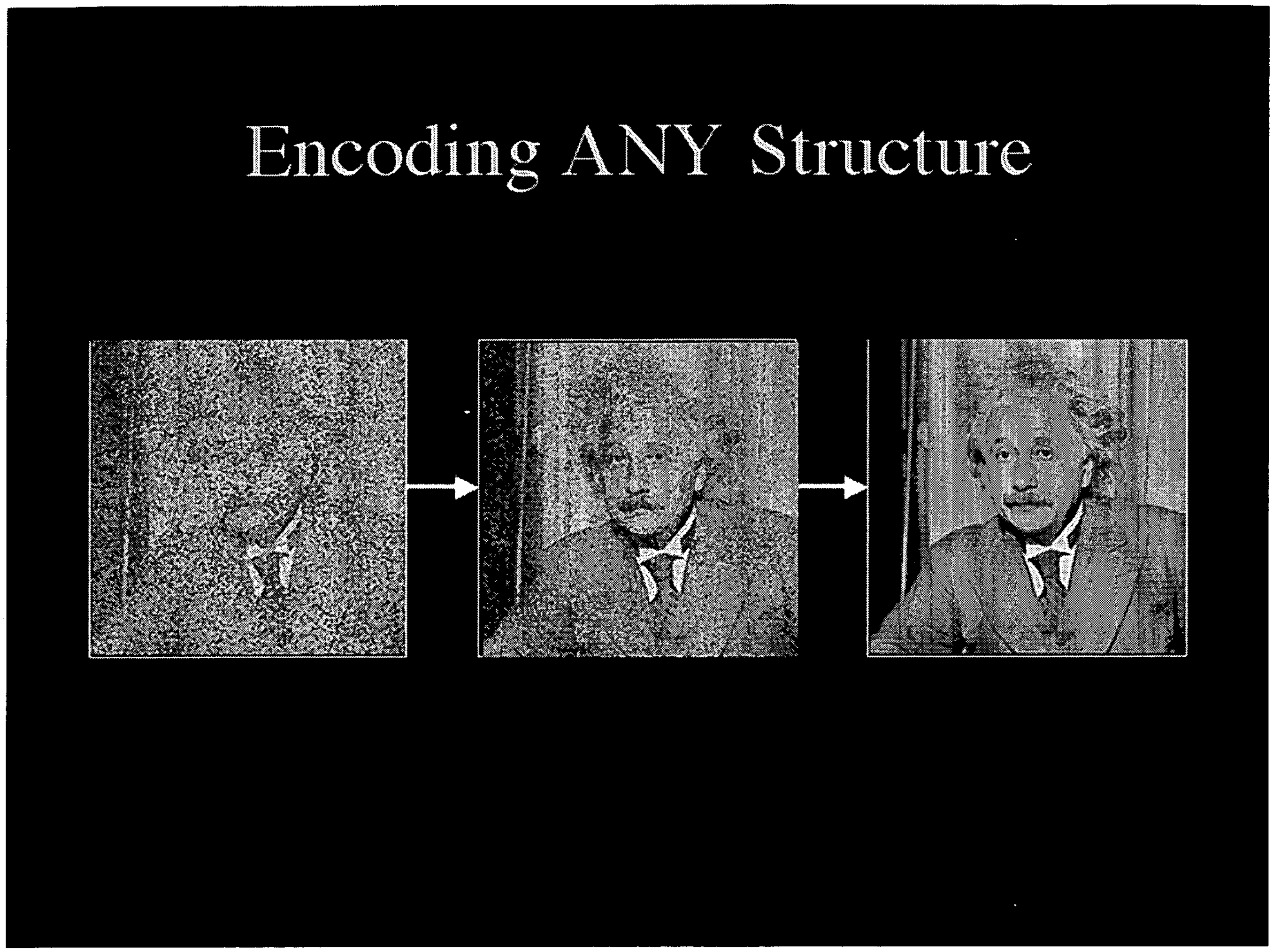
What does this mean? We may not need to conceptualize the existence of a plan prior to the realization of an object. Unlike a painter, for example, who conceives of an image and then executes it, there need be no pre-existing concept or plan to explain the appearance of an object. The object may actually organize itself into a complex pattern. Such a thing is impossible in linear systems.

Slide 29: Encoding Any Structure (1)



I want to make it clear that the idea of self-organization as a consequence of random implementation of a few rules has great generality and can explain the structure of any object. For example, the panel on the left is a completely random distribution of black and white dots. In this case I chose a set of approximately 400 rules and applied them randomly to compartments within this noise pattern. Each time the rules were applied, the appearance of the points within the compartment was altered as defined by the rules. The middle pattern shows some evolution toward a pattern, and the panel on the far right shows a little more progress.

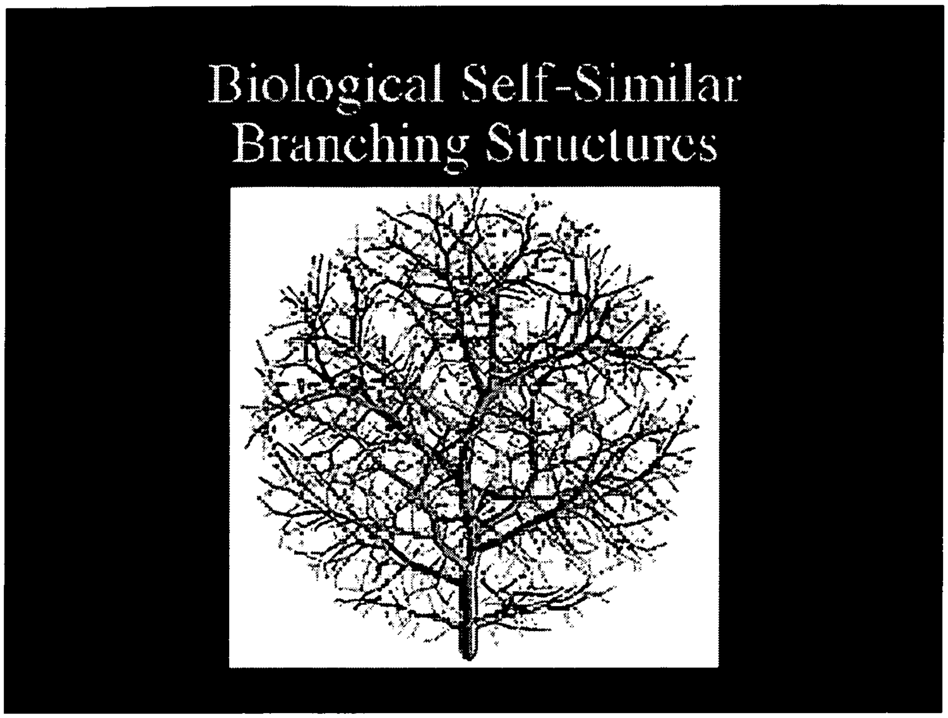
Slide 30: Encoding Any Structure (2)



As I continue to apply the rules to the compartments, you can see the particular result of the process.

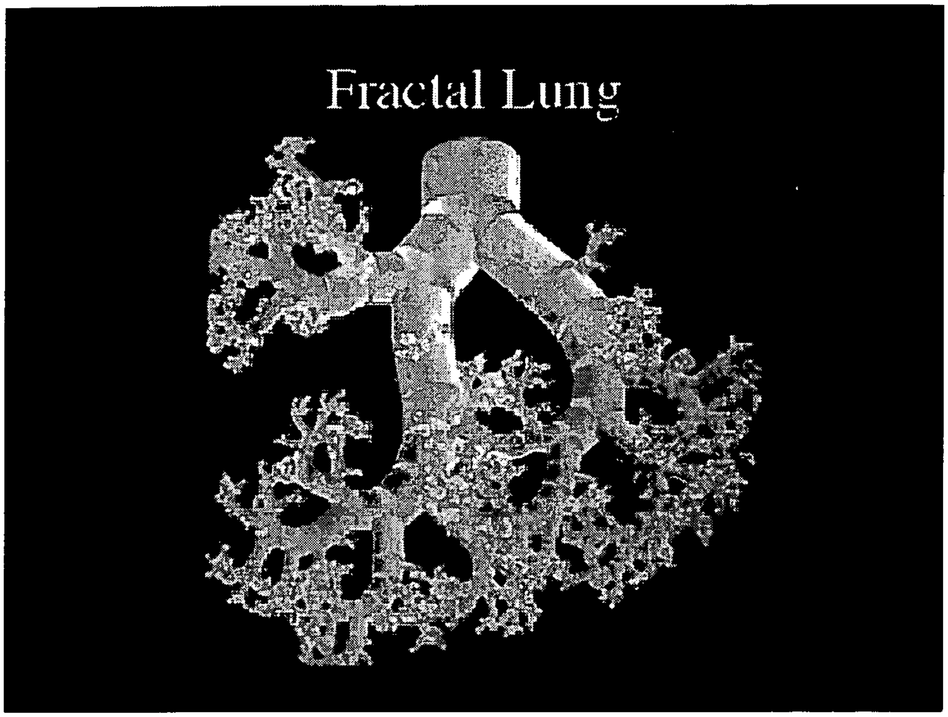
It took 400 rules to specify this image. But there might be 4000 chemical reactions going on in each cell in the body, so 400 rules is not an unusually great number. The process of creating the image involved the notion of compartments, but that is exactly how cells are constructed. There are discrete compartments within cells and specialized reactions within these compartments. All the rules required for this image were implemented randomly. Thus, again, we see that self-organization can occur without the need for a pre-existing concept that channels and guides the process.

Slide 31: Biological Self-Similar Branching Structures



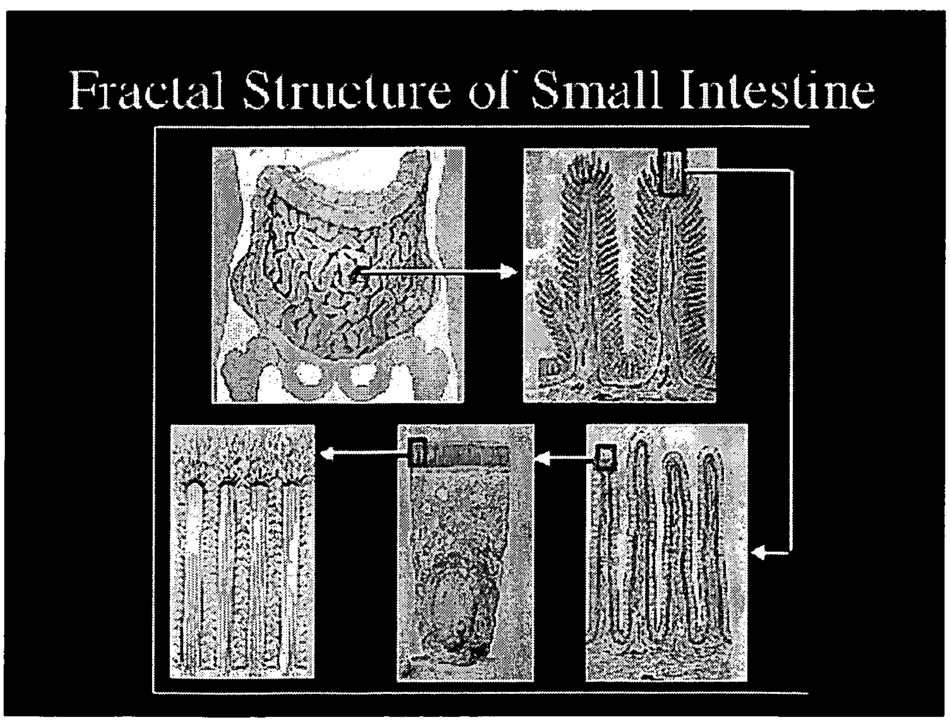
I now want to turn my attention from nonlinear biological activity to the idea of the consequences of nonlinear activity. Although we have not recognized or employed the fact significantly thus far, numerous living objects display the highly non-Euclidean form of geometry that we call self-similarity. The class of structures that show branching is a good example. These structures branch to form smaller limbs, which in turn branch to form still smaller limbs. Unlike mathematical branching structures which show this property over an infinite number of levels, biological structures do so only over a fixed number of levels - perhaps 5 or 10, depending on the particular biological structure involved.

Slide 32: The Fractal Lung



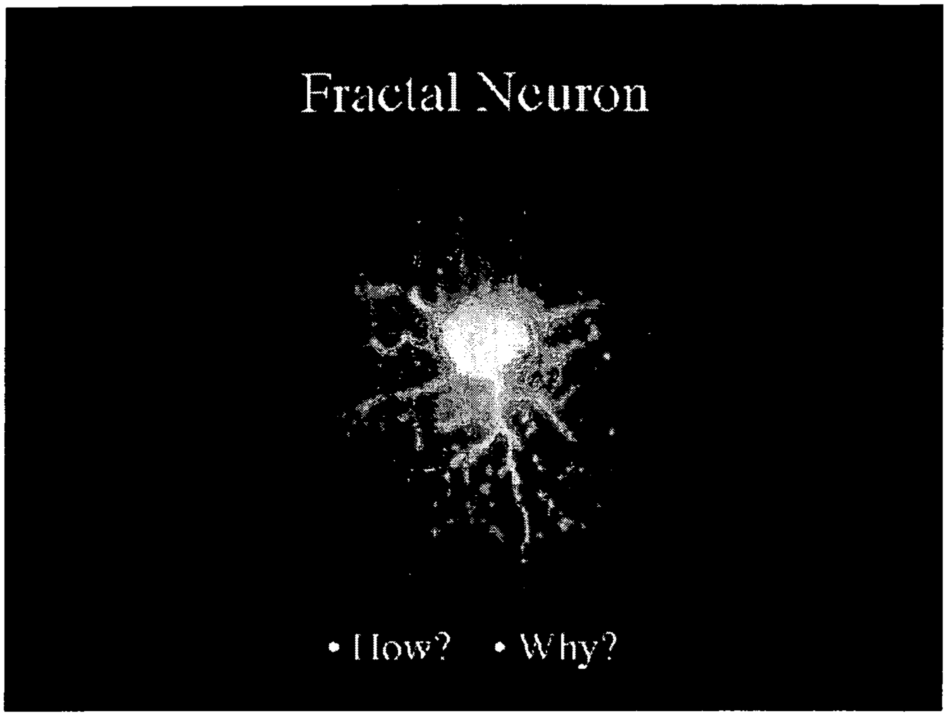
This is a depiction of the 3-dimensional structure of the lung, and again we see the basic pattern of self-similar branching.

Slide 33: Fractal Structure of Small Intestine



The intestine also exhibits the property of self-similarity. In this case, the inside surface of the intestine exhibits a finger-like structure, and each successive level of magnification reveals the presence of a similar kind of structure.

Slide 34: The Fractal Neuron



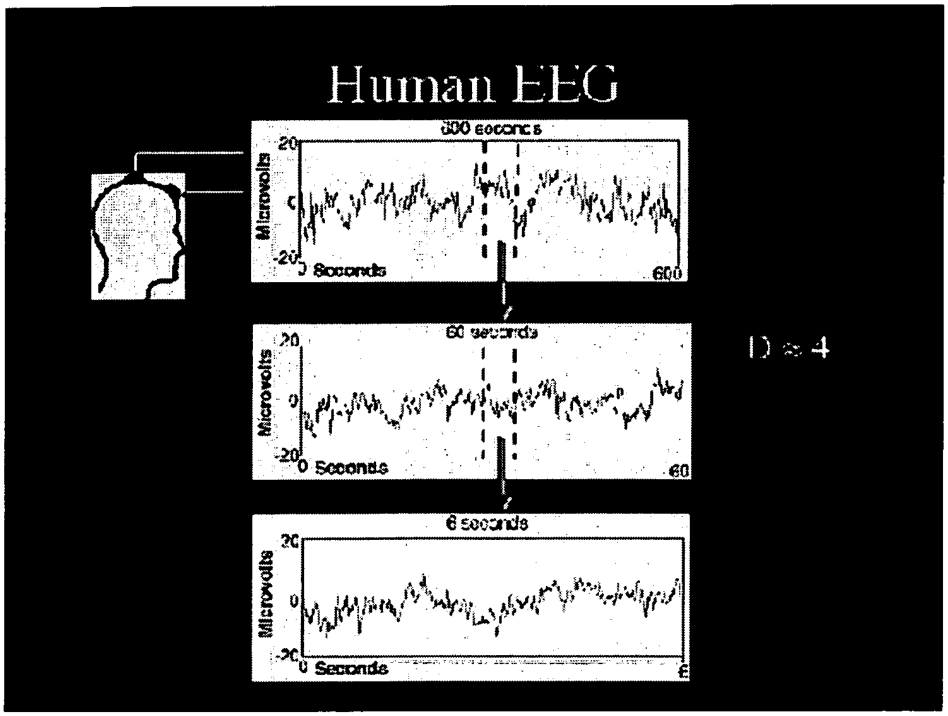
This is a photomicrograph of a single neuron - one nerve cell. You can see the body of the cell in the center, and the branching structures that emanate from it which serve to receive inputs and conduct outputs to other cells. This branching structure shows self-similarity and can be characterized by a fractal dimension.

How did these self-similar branching structures come about? A likely possibility is that they were formed by a nonlinear series of nonlinear chemical reactions. Linear modeling cannot explain self-similarity.

Why did nature choose self-similar geometries so frequently? I could show that these structures are maximally efficient. Take the example of the intestine. If you were asked to design a geometry for a surface that would fit within a fixed volume but would have the property of maximizing the surface area, hence maximizing nutrient flow from the lumen of the intestine into the bloodstream, then it turns out that the self-similar fractal structure is exactly the geometry that maximizes the nutrient transfer process. Similarly, if the goal were to maximize transport of oxygen across a surface within a volume or to maximize the number of inputs the particular neuron could receive from other cells, the structure that best accomplishes the task is a self-similar structure.

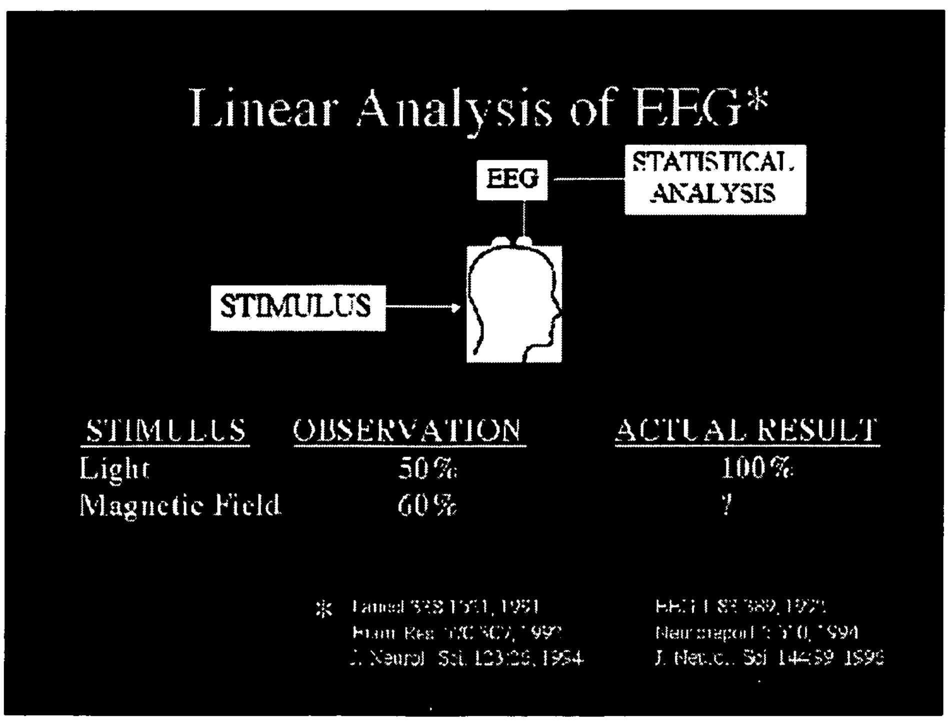
Thus self-similar biological structures probably evidence the operation of nonlinear laws and are an optimal design from an evolutionary standpoint.

Slide 35: Human EEG



Now I want to consider some applications of nonlinear thinking. The top panel shows about 600 seconds of human EEG data that I obtained. The EEG is a self-similar signal, and this can be demonstrated in the same manner as I demonstrated self-similarity in the mathematical model of the weather. The fractal dimension of the signal is about 4.

Slide 36: Linear Analysis of EEG

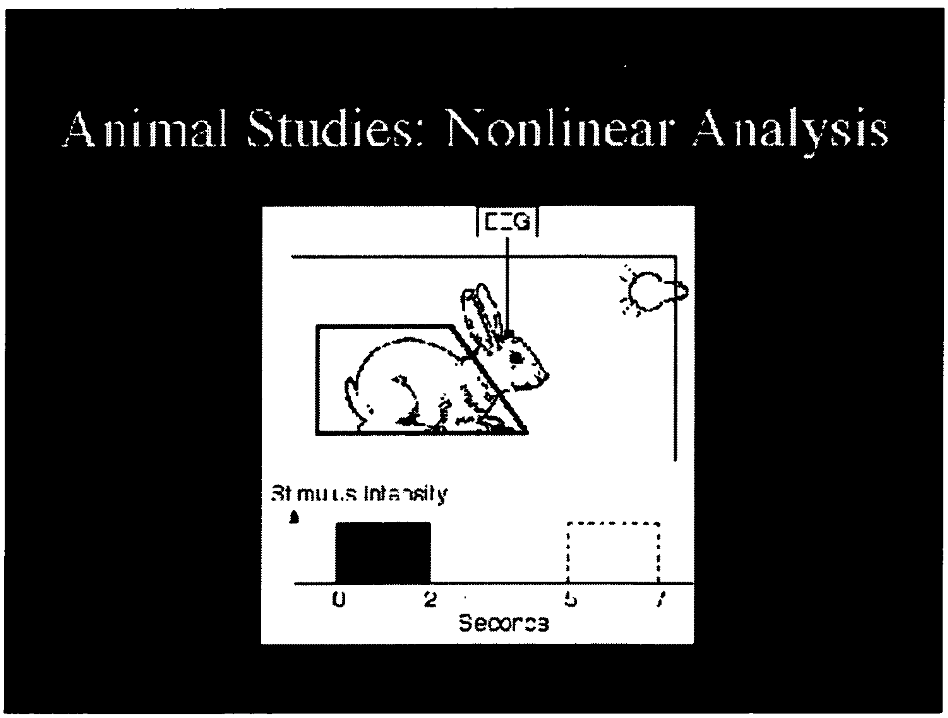


In a series of studies I analyzed animal and human EEG signals using traditional linear methods. The purpose

was to detect changes in the EEG that occurred as a result of a stimulus. These experiments were done in such a way that it was possible to assess whether or not the stimulus affected the EEG in a particular subject. That is, the design did not involve averaging, but a determination of whether each individual subject did or did not respond to the stimulus. Many subjects were involved in these studies and about 50% were found to respond to a low-intensity light signal. That is, from an analysis of the EEG we could objectively demonstrate changes in the EEG that were due to perception of the light. This is about the same percentage as all previous studies had reported. We could be certain, however, that 100% of the subjects actually saw the light because we asked them, and they could describe when it was on or off. Thus, brain electrical activity was necessarily different when the light was on compared with when the light was off in all subjects tested, even though we could prove the difference existed in only 50% of the cases.

When we applied a low-frequency magnetic field we found that about 60% of the subjects detected the field as determined by responses observed in the EEG. In this case, however, we could not determine independently how many of the 40% apparent non-responders actually responded to the magnetic field. That is, we could not distinguish between a failure to respond to the magnetic field, which would suggest that some persons are sensitive to low-frequency fields while others are not sensitive. Alternatively, perhaps our detection system was not sufficiently sensitive to record responses in some subjects.

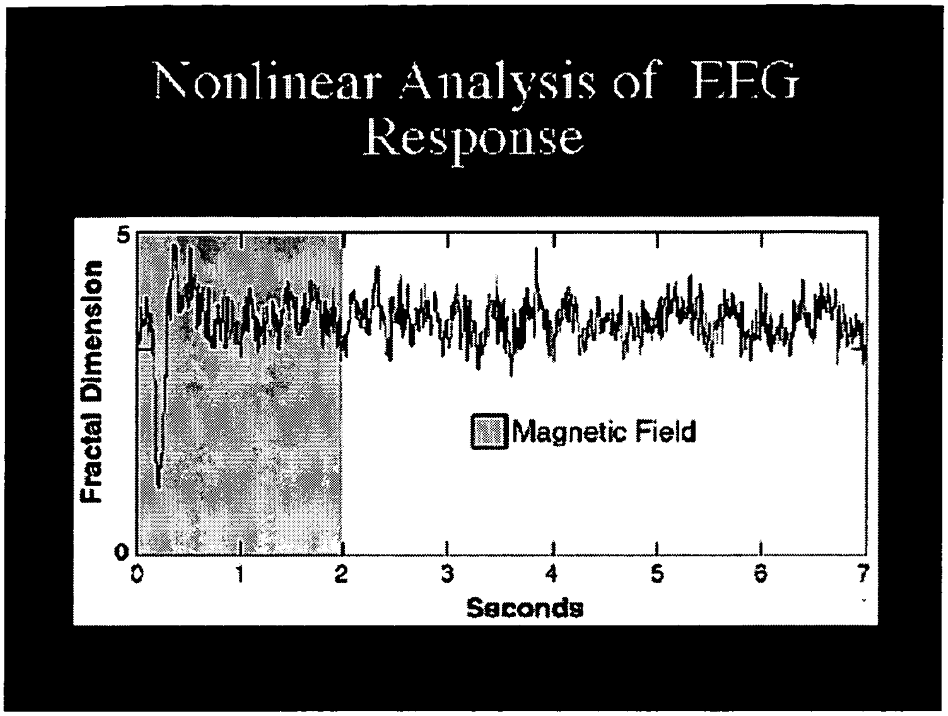
Slide 37: Animal Studies: Nonlinear Analysis



We hypothesized that sensitivity to low-frequency magnetic fields was really a universal property of human beings, and that failure to recognize detection in almost half the subjects studied was a result of our use of a linear model to try and understand what was basically a nonlinear phenomenon.

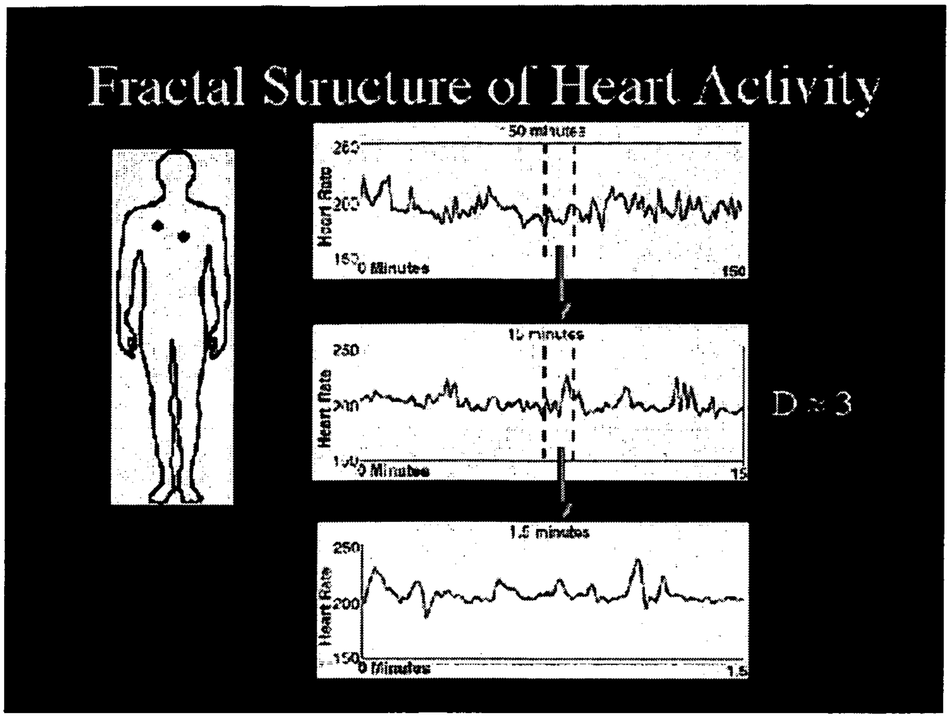
We then conducted animal studies. A stimulus was applied for 2 seconds, and off for the following 5 seconds. The process was repeated for a total of 50 trials. We compared the EEG measured during the stimulus with the EEG measured during a control period, which we chose as the last 2-second interval prior to application of the stimulus in the next trial.

Slide 38: Nonlinear Analysis of EEG Response



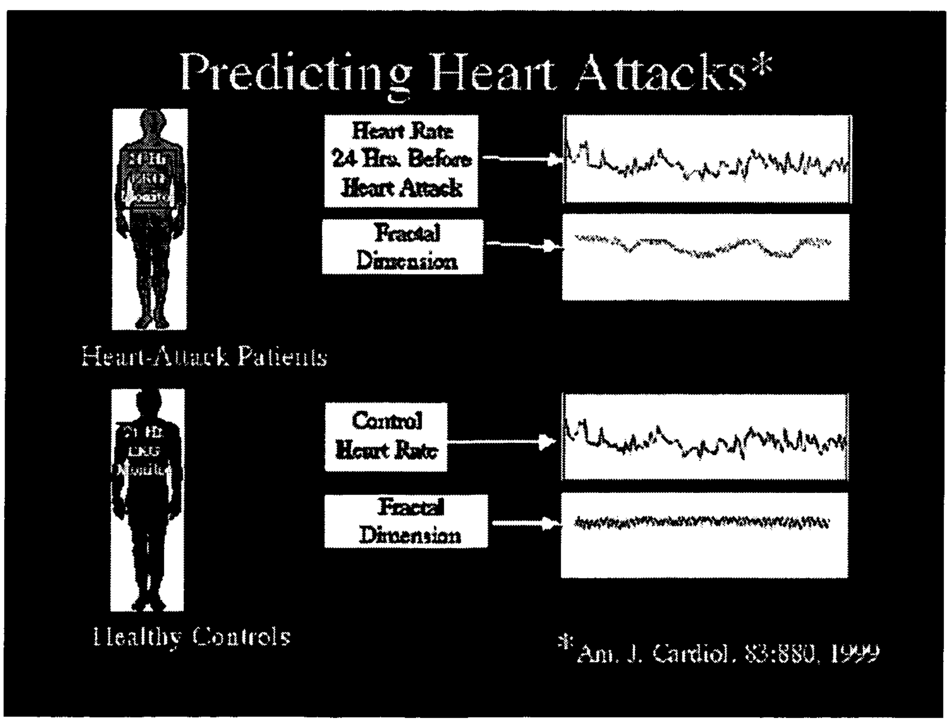
This is the result I obtained. Upon application of the stimulus, either light or magnetic field, the fractal dimension of the EEG decreased precipitously, clearly indicating the fact that the animal responded to the presence of the stimulus. The change was maximum about 300 msec after initiation of presentation of the stimulus. Thereafter, even during the latter portion of the time the stimulus was applied, the fractal dimension returned to its baseline range. This decrease in fractal dimension occurred with every rabbit that we studied. Similar human studies are presently underway.

Slide 39: Fractal Structure of Heart Activity



I recorded a human electrocardiogram and processed the data to show heart rate over 150-minute interval. Analysis confirmed the observations of others and showed that heart activity was fractal, with a fractal dimension of about 3.

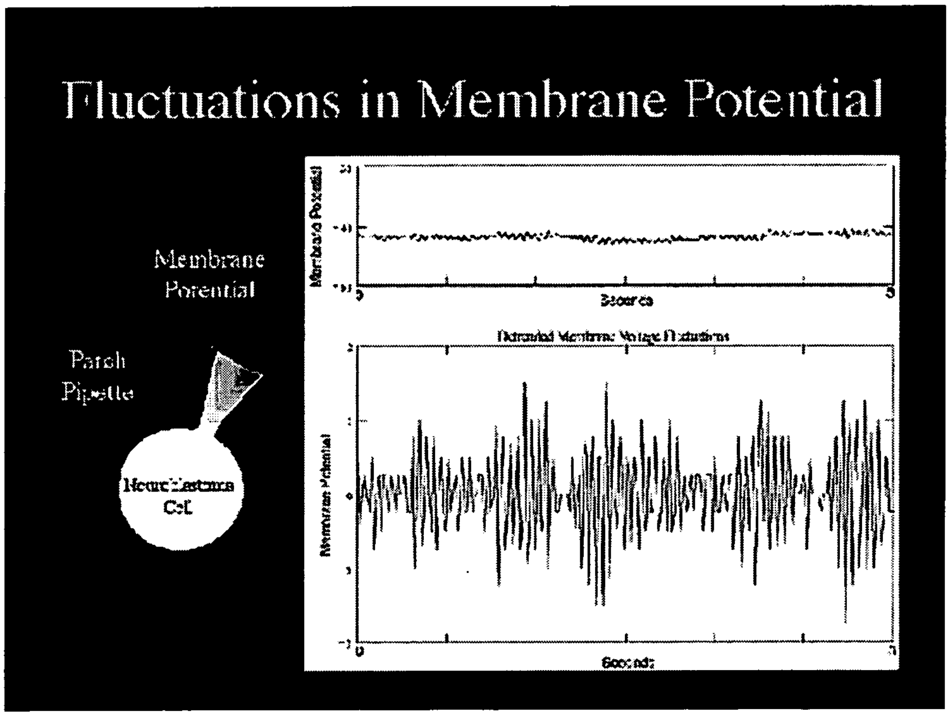
Slide 40: Predicting Heart Attacks



This is data from a study published recently. The subjects in this study wore a device that monitored their heart rates continuously over a 24-hour period. Some of the monitored patients spontaneously developed heart

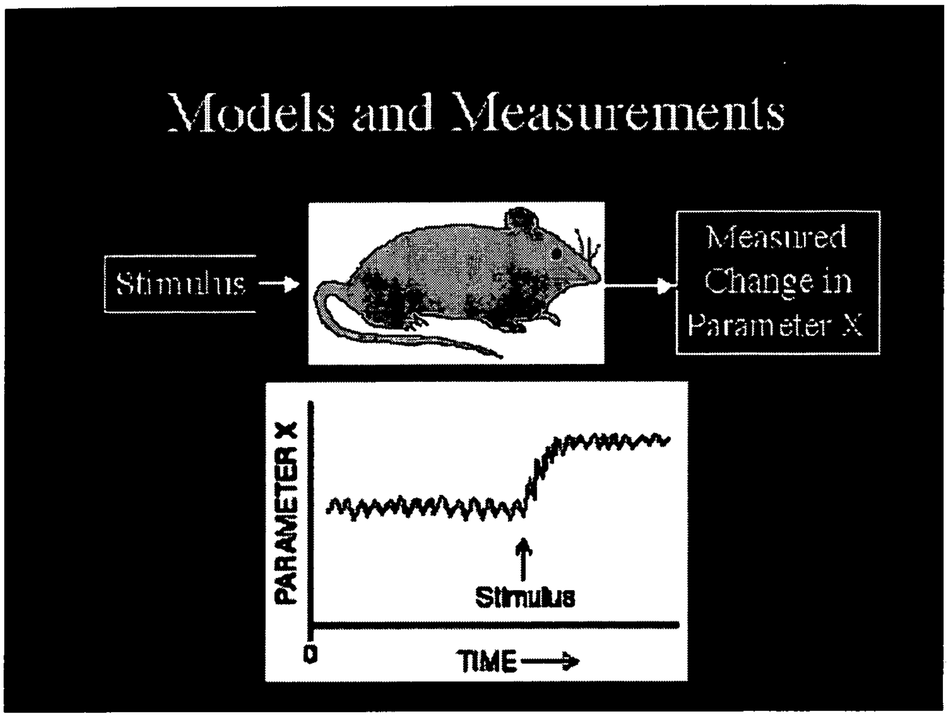
attacks, and the heart rate of a typical heart attack patient is depicted in the top panel. A corresponding panel illustrates the heart rate in a healthy control subject. It was found that the patterns were apparently identical when examined using a linear model. However, when the data was examined using a nonlinear model, spontaneous decreases in fractal dimension were observed in all of the patients that progressed to a heart attack. This behavior occurred hours prior to the heart attach and was not seen in any of the healthy controls. It appears, therefore, that it may be possible to actually predict individual subjects that are likely to experience a heart attack, and perhaps even to estimate when the heart attack may occur.

Slide 41: Fluctuations in Membrane Potential



I want to make it clear that nonlinear analysis is not confined to the macroscopic level. There is a bright possibility that nonlinear analysis of cellular and subcellular signals may be found to be a rich source of information about biological systems. For example, this slide depicts the measurement of the membrane potential of a cell in tissue culture. In this case I touched a glass micropipette to the outside of a cell, thereby forming a cell patch. I then destroyed the portion of the cell membrane that blocked the lumen of the pipette, thereby gaining electrical access to the inside of the cell. The top panel depicts the membrane potential measured under this condition, which was about -42 mV with small apparently random variations. However, when I focused in on the variations, I found that they were far from random and in fact exhibited a high degree of determinism. The existence of a fractal pattern is suggested by the amplified view shown in the bottom panel, and was confirmed by analyzing the signal using standard methods. Thus, it is possible that different kinds of cellular activity could be detected by analyzing nonlinear behavior heretofore ignored in measurements of membrane potential.

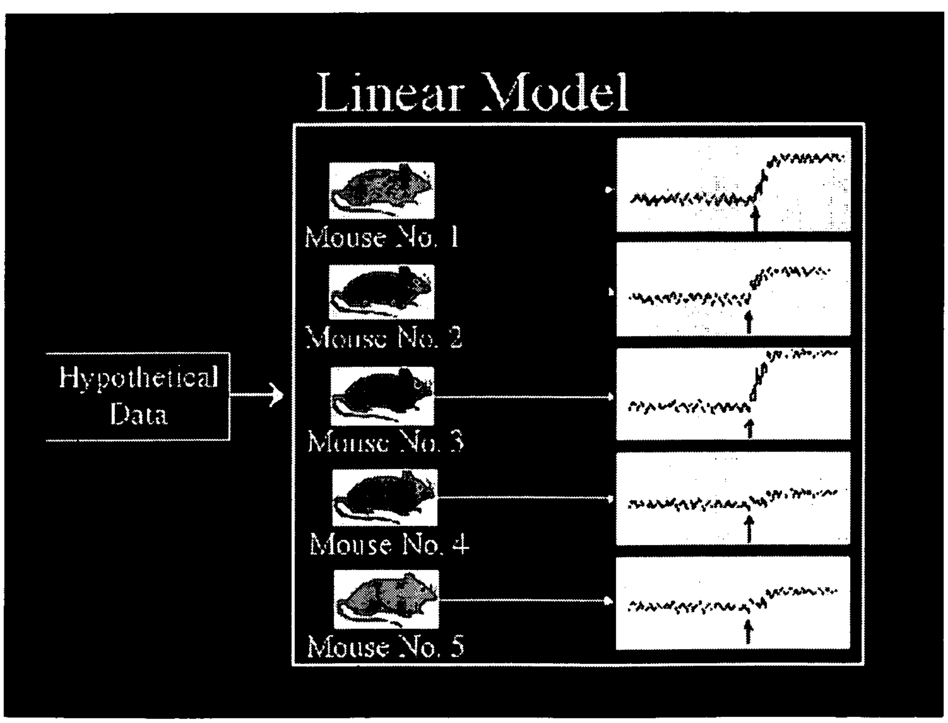
Slide 42: Models and Measurements



I want to describe one further example of an area where nonlinear concepts will, I think, be useful. This happens to be the area where my work is focused. To make my point, I need to discuss the way experiments are normally performed.

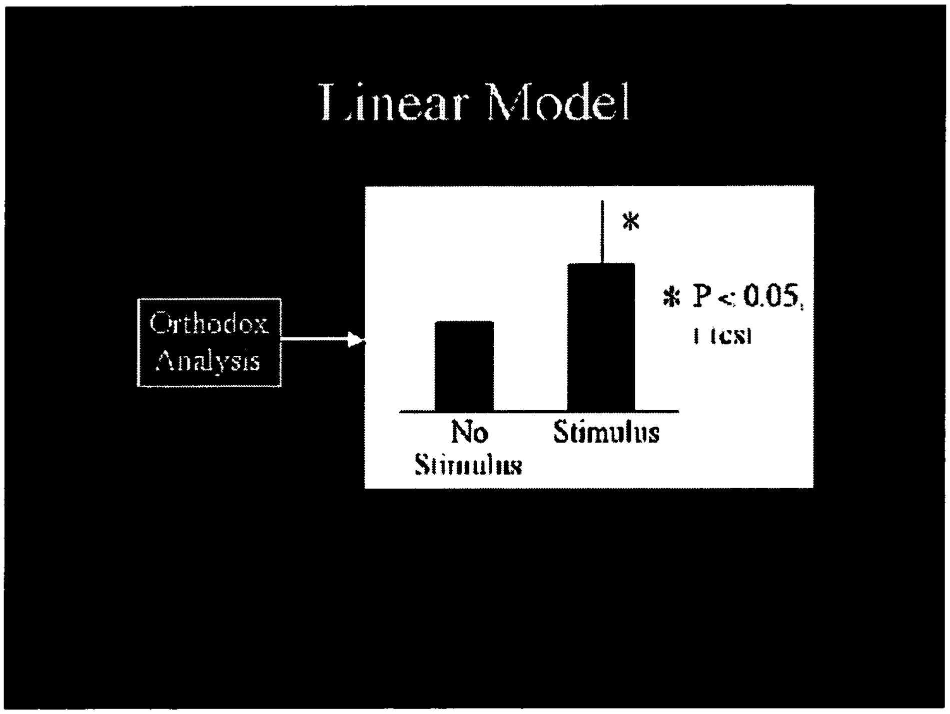
In a typical experiment in which we ask whether a given stimulus affects a particular parameter, a general procedure is to measure the parameter before and after application of the stimulus.

Slide 43: Linear Model (1)



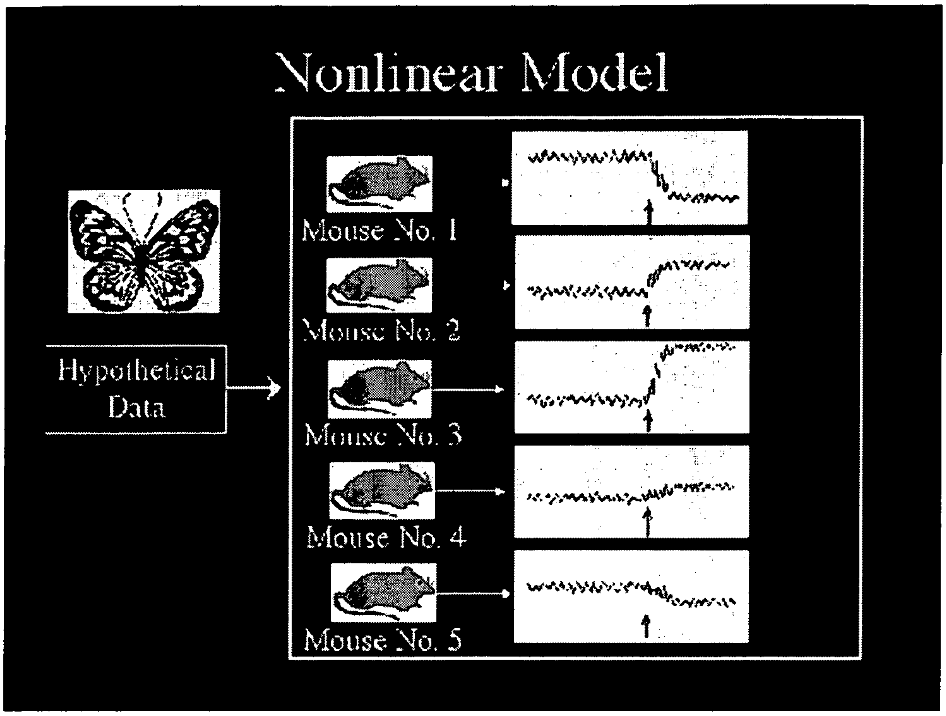
Because of biological variability, we do not expect to find exactly the same change with every animal. If we adopt a linear model, this is what we expect to see in order to report that a stimulus caused a change in the parameter. The amount of the change need not be exactly identical in every animal but (1) the change should occur in every animal or at least most animals, and (2) it should be in the same direction in every animal, or at least in most animals. The higher the percentage of animals that show a response and the higher the percentage of animals that show a response in the same direction, the better we like the results.

Slide 44: Linear Model (2)



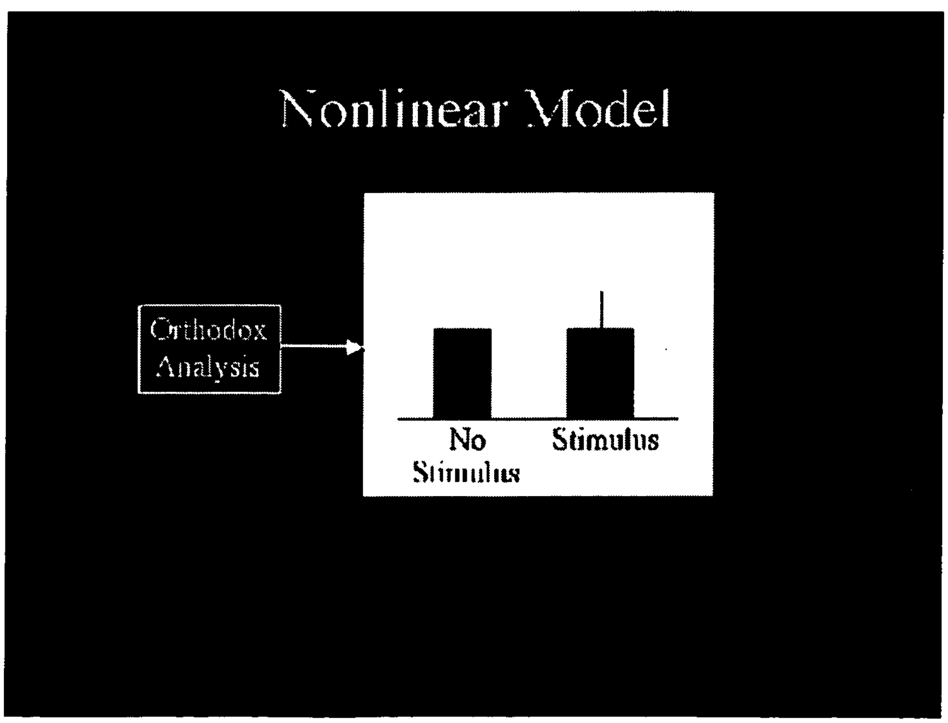
This shows the results of a typical analysis of such data. There is some variability in the data whether or not the stimulus was present, but on average, the stimulus showed greater value and the difference was "statistically significant."

Slide 45: Nonlinear Model (1)



What result do we expect if a nonlinear model is actually correct? In this case, it is entirely possible that some animals may not respond at all and that the remaining animals may respond by different amounts in different directions. That is, if a nonlinear model were truly applicable, then the result in any particular case would not be predictable.

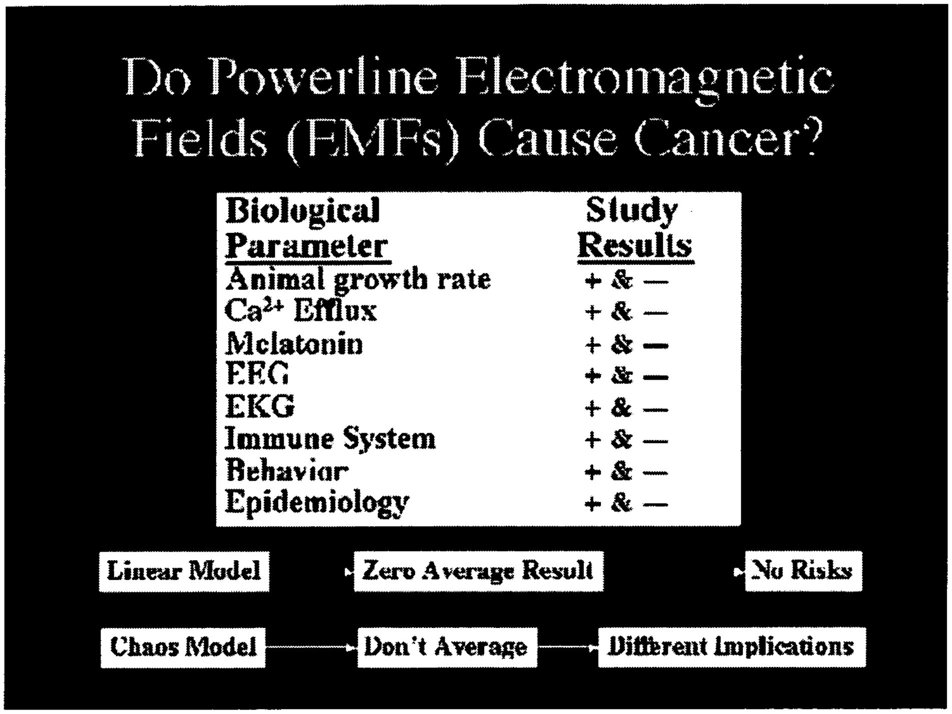
Slide 46: Nonlinear Model (2)



If we did an orthodox analysis of data generated by a nonlinear process, we would conclude that the stimulus

was without effect because, on average, the value of the parameter was the same in both cases. But I already assumed in the previous slide that in virtually every case the stimulus did have an effect on the parameter. Thus, it can be seen that insistence on a linear model to interpret data can be highly misleading when the underlying dynamics are actually nonlinear.

Slide 47: Do Powerline Electromagnetic Fields (EMFs) Cause Cancer?

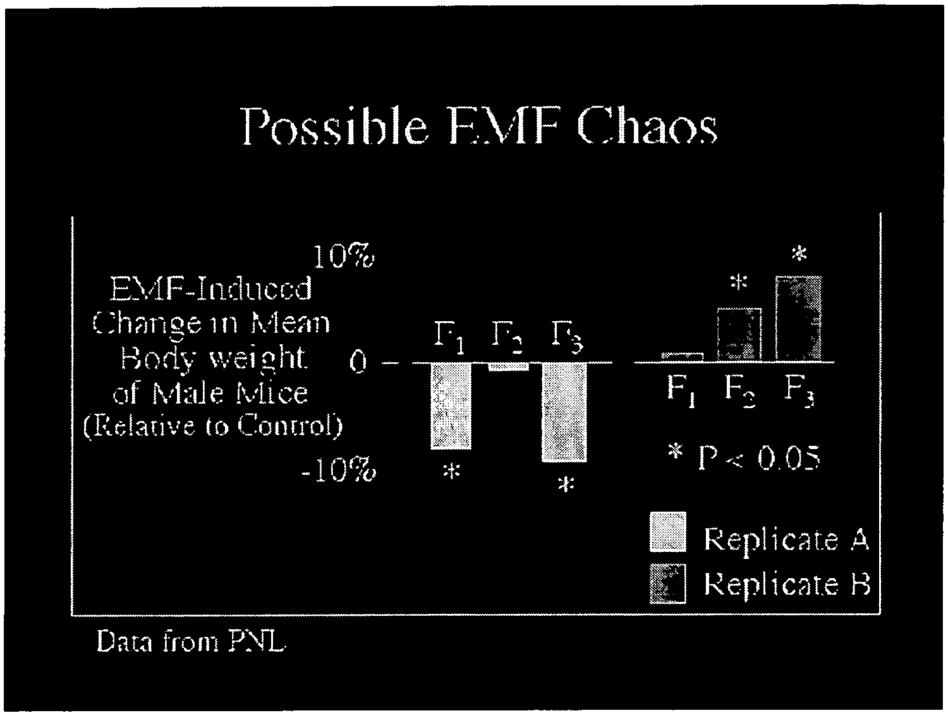


I now want to make the point that the distinction I just drew between linear and nonlinear modeling is not a mere academic one but rather is at the core of how we understand our world and, in particular, how we understand what causes cancer.

Many people reside near high-voltage powerlines, and the question arises whether, as some have suggested, long-term exposure to the fields from these lines causes cancer. In an attempt to understand how that might possibly come about, many scientists have done laboratory studies in which many different parameters were measured. I have listed a few of them here. In these cases, and in virtually every other case, one can find studies in which parameters were found to be affected by fields, as well as studies in which such effects were not found. What is the significance of these observations? If one chooses to apply a linear model to interpret the data, then it is easy to conclude that, on average, the fields had no effect. This being true, it would follow that the fields could not be a risk factor for disease and the companies that operate the powerlines would therefore have no moral or legal liability for causing disease.

On the other hand, if one examines the data from the framework of deterministic chaos, the results would not be averaged because it is clear that such a procedure would average away real effects. The implications regarding whether powerlines caused disease would, consequently, be vastly different than was the case with application of the linear model.

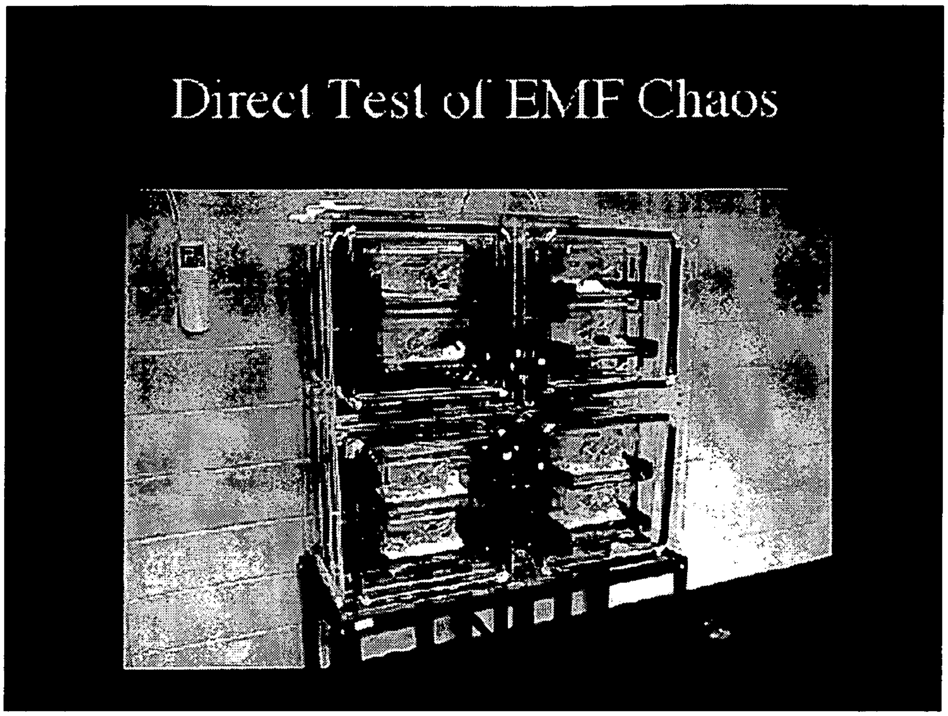
Slide 48: Possible EMF Chaos



Here is an example of published data that illustrates the point I just mentioned. This data was obtained by investigators at Battelle Pacific Northwest Laboratories in Richland, Washington while under contract to the Electric Power Research Institute and the Department of Energy. The experiment consisted of mating and rearing mice while they were exposed to power-frequency electromagnetic fields. The offspring of the first generation (labeled F1) were in turn mated to produce a second generation (F2), and they were used to produce the final (F3) generation. Similar procedures were carried out with control animals, and the data is shown in yellow. The entire procedure was repeated, and the data from the replicate study is shown in green. The slide shows results only from male mice, but the results from the females were similar. The investigators found that the mice in the first generation that were exposed to the field were statistically significantly lighter than the corresponding controls, about 8% on average. In the second generation the difference was much smaller, but not statistically significant. In the third generation, however, the results were again statistically significant. However, when the experiment was repeated it was found that he second and third generations were statistically significantly heavier than the corresponding controls. If one accepted a nonlinear model, then the data would be interpreted to say that living in a power-frequency electromagnetic field affected the growth rate of the mice, but that the direction of the effect was influenced by unknown factors. The investigators, however, chose to apply a linear model and averaged the results of both experiments to conclude that the data showed no effect due to the EMFs.

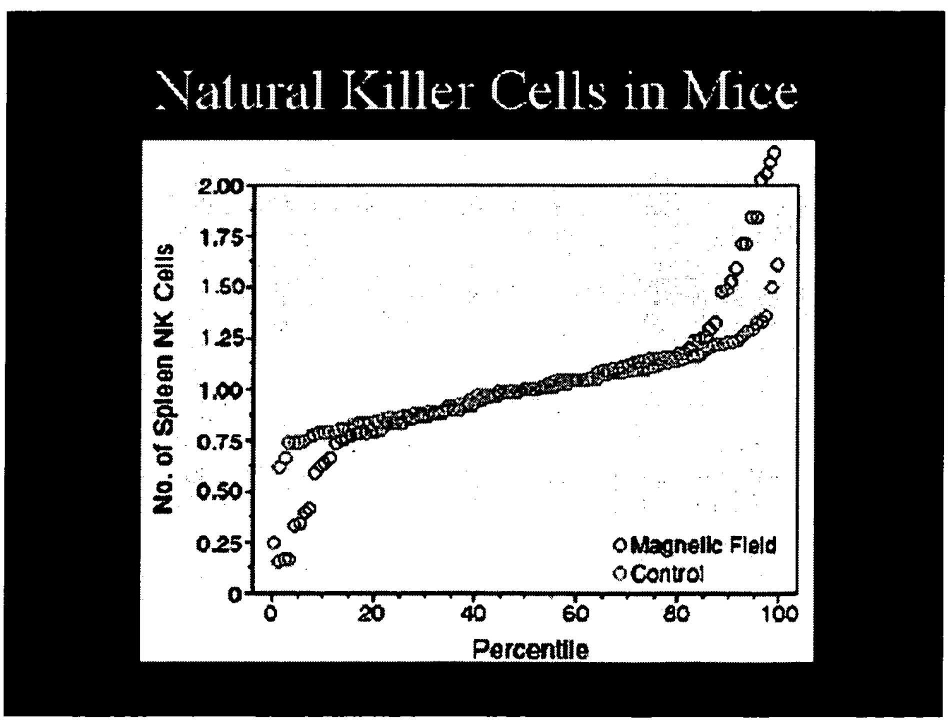
It is clear, consequently, that the data does not speak for itself. Rather, what it says can actually be controlled by what model one chooses to apply.

Slide 49: EMF Exposure System



My view is that the proper interpretation of the Battelle data is the interpretation that they rejected, and for the last 4 years I conducted a study aimed at directly testing my hypothesis that EMF-induced bioeffects are nonlinear in nature. I designed and built this apparatus which permitted me to expose mice to a precisely controlled magnetic field. The mice lived in a totally non-metallic environment and were exposed to a precisely known field strength. Similar units were built to house control mice.

Slide 50: Natural Killer Cells in Mice

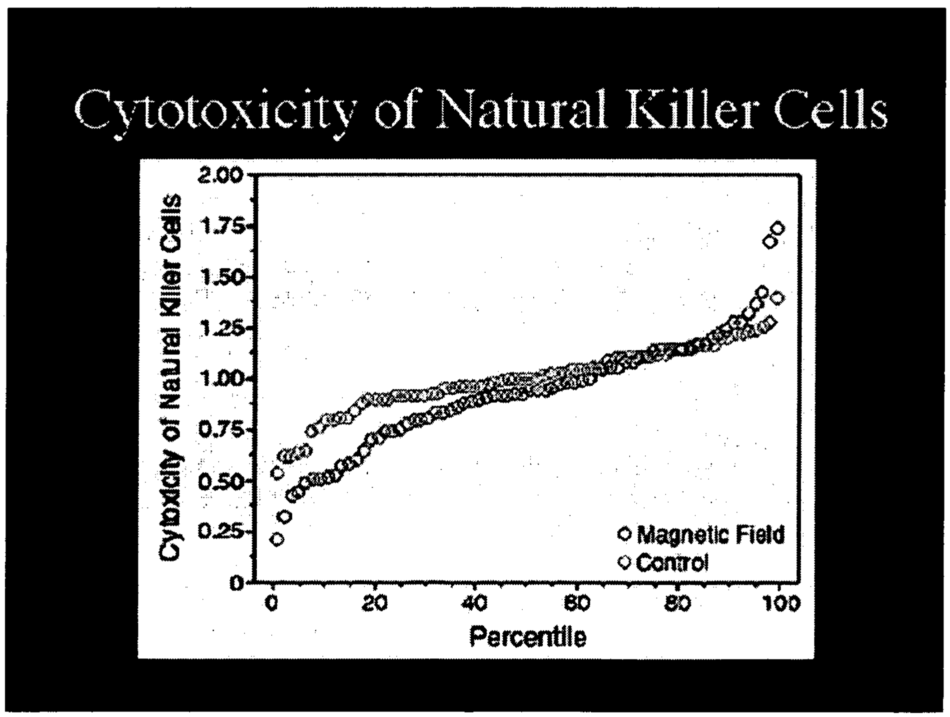


In these studies mice, both males and females, were exposed to fields of varying strengths for varying periods of time, and a total of 20 immune parameters were measured in each animal. The results of these studies have not yet been published, but I can easily describe the kind of results that I obtained, and it will be clear that my idea that the responses were nonlinear was fully supported.

Among the parameters that I measured were two parameters that characterized a particular lymphocyte subset known as natural killer cells. These cells are part of the body's immunosurveillance mechanism, and I had hypothesized that they would be particularly susceptible to the presence of a magnetic field. This slide shows some of the results I obtained following exposure of female mice to 5 gauss, 60 Hz, for various periods of time up to 105 days. Each circle depicts the result obtained from a specific mouse, and the results from both the exposed and control animals were arranged in percentiles because that method of data presentation is particularly suited to demonstrating the existence of nonlinear effects.

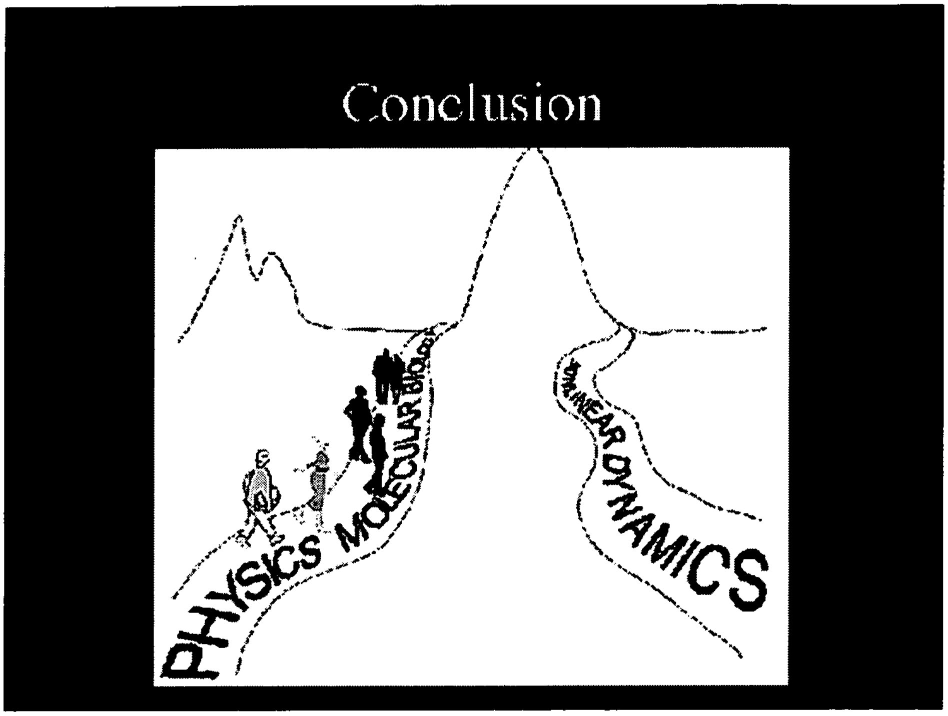
You can see that the differences caused by the field involved the animals whose values fell at the extremes of the distribution. The EMF produced effects, and it was these animals that were affected. You can see intuitively that if the results were averaged, the conclusion would be that the field had no effect.

Slide 51: Cytotoxicity of Natural Killer Cells



The previous slide demonstrated the nonlinear effect of the field on the numbers of natural killer cells. The cytotoxicity of natural killer cells is an independent parameter related to the functional ability of these cells to kill tumor cells. Again, I found that the effect of the exposure occurred on animals at the tails of the distribution. Again, if the results were averaged, the incorrect conclusion would be that the field produced no effects.

Slide 52: Conclusion



The deductive style and emphasis on equations capable of predicting specific observations was developed by physicists, particularly in the last 100 years, and it became the dominant paradigm for science. Biology, when it grew up, would be like physics is the implication that one frequently finds in standard textbooks describing experimental methods. But physics is now a dead science. All of the deep laws of nature have been discovered. We know this is the case because there do not appear to be any physical phenomena that anyone really believes would require new laws. Physicists are now largely marginalized to tasks that appear to have no direct significance for the future of humanity. All of the great physicists who ever lived are already dead. The new paradigm that replaced physics is molecular biology. It consumes a vastly greater portion of national scientific budgets, has a much greater claim on the public mind, and appears to have a much greater possibility of improving the human condition. But molecular biology is inherently limited because it is a technique, not a science. Molecular biology does not explain anything, it simply provides tools to answer particular questions. Many of the questions amenable to its methodology are of great interest, and it is entirely possible that the greatest molecular biologist who will ever live has not yet been born. But, even now, we can recognize limitations in the molecular biology methodology, and we can see that certain kinds of questions cannot be asked within its framework. For this reason, it seems to me, that the next paradigm will involve a combination of mathematics, physics, and molecular biology, integrated into a way of looking at nature that we recognize and ultimately come to understand its nonlinear dynamical nature.

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